NEW RESEARCH

NEW RESEARCH ABSTRACTS

AMERICAN PSYCHIATRIC ASSOCIATION

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ABSTRACTS

NR1 Monday, May 22, 9:00 AM - 10:30 AM

Cognitive and Social Functioning in Recovery From Depression: Results From a Population-Based Three-Year Follow-Up

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to consider depression as a serious disorder also in population-based samples. We found that despite the symptomatic improvement and improved social functioning, cognitive functioning does not follow this recovery trend. This finding suggests that depression can cause long-standing neurobiological impairments which may have major public health implications.

Summary:

Objective. Although it is well established that depression is associated with cognitive dysfunction, few studies have investigated recovery of cognitive performance as a function of recovery from depression. In contrast, it is well documented that depression is associated with social disability. In order to explore this further, we used longitudinal data from the PART project in Stockholm, Sweden.

Method. A population-based sample of individuals diagnosed with depression as defined in DSM-IV were examined twice with a tree year retest interval. Psychiatric data (Schedules of Clinical Assessments in Neuropsychiatry), information on social disability (WHO's Brief disability Questionnaire), and cognitive data including tests of episodic memory were obtained from 76 respondents both at baseline and three-year follow-up. In addition, background data concerning demographic factors, anxiety level, alcohol and drug use were considered.

Results. The sample was divided into those who did (n=41) and did not fulfill (n=35) the criteria for DSM-IV depression at follow-up examination. These two groups were compared with respect to social disability and episodic memory performance at baseline (T1), at follow-up (T2) and across time (i.e., by examination of residual change scores). Results revealed that the study samples did not differ in episodic memory performance either at T1, T2 or residual change whereas the groups differed in social functioning at T2 and with respect to residual change such that the group that had recovered from their depression also demonstrated improved social functioning.

Conclusion. The results suggest that depression is a serious disorder where, despite the symptomatic improvement and improved social functioning, cognitive functioning does not follow this general recovery trend, at least not in the three-year interval examined. It is speculated that depression may cause long-standing cognitive deficits.

References:

1. Weiland-Fiedler P, Erickson K, Waldeck T, Luckenbaugh DA, Pike D, Bonne O, Charney DS, Neumeister A. Evidence of continuing neuropsychological impairments in depression. J Affec Disord 2004; 82: 253-258.

2. Neumeister A, Wood S, Bonne O, Nugent AC, Luckenbaugh DA, Young T, Bain EE, Charney DS, Drevets WC. Reduced hippocampal volume in unmedicated, remitted patients with major depression versus control subjects. Biol Psychiatry 2005;57:935-937.

NR2 Monday, May 22, 9:00 AM - 10:30 AM

The Risk of Metabolic Syndrome Among Patients With Mood Disorders: Findings From the Western Part of Turkey

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize and try to prevent the metabolic syndrome in patients with mood disorders.

Summary:

Objective: The prevalence of metabolic syndrome (MS) in general population of Turkey is between % 20-30. The metabolic effects of psychotropics agents have been considerable debate. It is not clear whether individuals with mental disorders are at greater risk for obesity and metabolic syndrome than the general population even without taking antipsychotics.

The study sought to evaluate the presence of MS in a group of 143 patients with mood disorders who were recruited in the specialized mood disorder outpatient unit in Izmir, Turkey.

Methods: Data were collected from the patients with mood disorders (bipolar disorder, recurrent depression, and schizoaffective disorder). The study focused on the presence of MS as defined by the NCEP ATP III and risk factors associated with MS.

Results: 24.5 percent of the sample met the NCEP ATPIII criterion for the MS, 29.4% met the criterion for abdominal obesity, 38.5% met the criterion for hypertriglyceridemia or were on a cholesterol lowering agent, 61.5% met the criterion for lower HDL-cholesterol levels, 22.4% met the criterion for hypertension and 21% met the criterion for high fasting glucose or antidiabetic mediaction use. There was a positive correlation between the number of criterion for the MS and body mass index (r=0.482, p=0.0001). According the regression analysis, antipsychotic treatment (p= 0.032) and older age (p=0.009) are risk factors for the presence of the metabolic syndrome.

Conclusion: The results support the hypothesis that antipsychotic-treated patients appear to be at risk for metabolic syndrome and obesity.

References:

1. Fagiolini A, Frank E, Scott JA et al: Metabolic syndrome in bipolar disorder: findings for the bipolar disorder center for Pennsylvanias. Bipolar Disord 2005; 7: 424-430.

2. Kahn R, Buse J, Ferranni E et al: The metabolic syndrome: time for a critical appraisal. Diabetes Care 2005; 28:2289-2304.

NR3 Monday, May 22, 9:00 AM - 10:30 AM

Preventive Socio-Political Measures Proposed by Brazilian Psychiatrists:1900-1950

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Educational Objectives:

At the conclusion of this presentation, the participant should be aware of the importance of keeping an analytical approach to the scientific knowledge and continuously improving the scientific enterprise through multidisciplinary studies.

Summary:

Objective: During the beginning of the 20th Century, psychiatrists in Europe and America made several proposals to control and

prevent mental disorders in the general population. This study describes and analyzes the content and impact of socio-political measures proposed by Brazilian psychiatrists between 1900-1950.

Method: Primary sources, articles published in the lay media, scientific papers, and conferences delivered by Brazilian psychiatrists between 1900-1950, were identified and analyzed. The governmental answers to these proposal were also investigated.

Results: Psychiatrists proposed measures strongly based on the mental hygiene and eugenics principles. The most important proposals were the treatment of the syphilis, the control of alcohol trade, the ban of religions with mediumistic practices, the control of the *media*, eugenic sterilization of mentally ill patients, and the immigration prohibition of Africans and Orientals. All these measures were presented on the basis of just scientific evidence and not on prejudices. The government responded with some legislative acts that were not necessarily enforced. The syphilis treatment, the control of mediumistic religions and the preference for European immigrants were started.

Conclusions: The psychiatrists proposed several socio-political measures to prevent mental disorders, and some of them resulted in discrimination and exclusion. The fact that the psychiatrists presented themselves as just neutral and objective scientists advises us to have a respectful but critical approach to organized knowledge. The constant improvement and the recognition of limitations to scientific knowledge must be balanced against mystification and overenthusiasm.

This study was supported by a doctoral grant from the CNPq (National Council for Scientific and Technological Development)

References:

1. Moreira-Almeida A, Almeida AAS, Lotufo Neto F. History of Spiritist Madness in Brazil. History of Psychiatry 2005; 16:5-25.
2. Birley, JLT. Psychiatrists and Citizens. British Journal of Psychiatry 1991; 159: 1-6.

NR4 Monday, May 22, 9:00 AM - 10:30 AM

Two Year Pilot, Open-Label Adjunctive Study of Chromium in Therapy-Refractory, Rapid- Cycling Patients With Bipolar Disorder

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to discuss the mechanism of action and the role of chromium in bipolar disorder.

Summary:

Background: Chromium has been reported to be beneficial to patients suffering from depressive disorders. This is the first investigation of chromium in the acute and long-term treatment of bipolar patients.

Methods: We conducted an open pilot, trial of chromium chloride (CC) in 30 therapy refractory, rapid-cycling DSM-IV bipolar patients. CC was given in dosages between 600 to 800μg as add-on to mood stabilizers over a 2-year period. Patients were rated weekly for the first four weeks and monthly afterwards with the Clinical Global Impression Scale-BP (CGI-BP), Hamilton Depression Rating Scale (21-item version) (HMDS-21), Montgomery-Åsberg Depression Rating Scale (MADRS) and Young Mania Rating Scale (YMRS). The first three weeks were separately analyzed for acute antidepressant effects. The mean follow up was 212±260 days (range:12 to 904 days).

Results: 30% in HAMD and 39% in MADRS of the patients were considered responders duringthe acute depressive phase. Regarding prophylactic effects, only seven patients (23%) could be followed up for one year and four patients (13%) could finish the study regularly. CC was well tolerated.

Conclusions: Chromium chloride may have some antidepressant properties, but failed to stabilize therapy refractory, rapid-cycling bipolar patients.

References:

1. Docherty JP, Sack DA, Roffman M, Finch M, Komorowski JR : A double-blind, placebo-controlled, exploratory trial of chromium picolinate in atypical depression: effect on carbohydrate craving. J Psychiatr Pract 2005; 11:302-314.
2. Liu PS, Lin MK : Biphasic effects of Chrom compounds on catecholamine secretion from bovine adrenal medullary cells. Toxicology 1997; 14:45-53.

NR5 Monday, May 22, 9:00 AM - 10:30 AM

Marital Satisfaction of Resident Physicians at the University of Puerto Rico

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Educational Objectives:

At the conclusion of this presentation the participant should be able to describe the marital satisfaction of resident physicians at the University of Puerto Rico; taking into account gender, specialty, post graduate year(PGY level) and other demographic factors. The participant should also be able to demonstrate broader knowledge of the instruments available to assess marital satisfaction. They will also increase their awareness about the importance of marital satisfaction in a resident's' life.

Summary:

Studies regarding marital satisfaction of physicians, suggest that demands of this profession affect family and couple relationships. Physicians, who report higher levels of marital satisfaction, report higher levels of family competence, work satisfaction and fewer psychiatric symptoms.

The purpose of this investigation was to describe the marital satisfaction of resident physicians at the University of Puerto Rico, and determine possible differences in marital satisfaction between residents in surgical and non-surgical specialties, gender and other demographic data. To obtain our data we administered the Dyadic Adjustment Scale (DAS), accompanied by a demographic information form, to married resident physicians in our system.

Ninety-one percent of possible subjects (n=179) participated in the study. Gender distribution was 60% male and 40% female. Surgical residents comprised 39% of the participants, while 61% belonged to non-surgical specialties. The group's mean scale value for marital satisfaction was found to be average. Residents scored highest in the dyadic cohesion subscale (common interests, and shared activities) and lowest in the dyadic satisfaction subscale (tension, present state of the relationship). Subjects with active religious participation obtained higher scores than those not active. Those with physician spouses obtained higher scores if the spouse was also in training. No correlation was found between the degree of marital satisfaction and age, number of children, ethnicity, religious affiliation, years of marriage, previous marriages, post-graduate year, or marriage to another physician. No statistically significant difference in marital satisfaction was found, between surgical and non-surgical residents (X^2=7.93, p= 0.24), nor between genders (X^2=6.04, p=0.42).

Despite the fact that our subjects obtained an average score on marital satisfaction, their score on the dyadic satisfaction subscale was lower when compared to other subscales. Attention should

be placed on diminishing tension and improving current state of the marital relationship if we interested in increasing the well being of resident physicians.

References:

1. Lewis JM et al.: Marital Satisfaction in the Lives of Physicians. Bulletin of Menninger Clinic 1993, 57(4):459-465.
2. Harari E: The Doctor's Troubled Marriage. Australian Family Physician 1998; 27(11):999-1004.

NR6 Monday, May 22, 9:00 AM - 10:30 AM

Symptom Subgroups as Endophenotypes in Genetic Studies of OCD

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to: 1) Define the concept of "endophenotype", 2) Understand how symptom subgroups derived from factor analysis can be used as endophenotypes, and 3) Understand how endophenotypes were used in this study to help identify associations between obsessive-compulsive disorder and genetic variants in the glutamate and serotonin systems.

Summary:

Background: Genetic factors are believed to play a major role in the etiology of OCD. Symptom subgroups of OCD have been proposed as "endophenotypes" that are more genetically homogenous than OCD diagnosis and therefore useful in the identification of susceptibility genes. We set out to determine if candidate genes from the 5HT and glutamate systems are associated with OCD symptom subgroups. Methods: We studied 160 adult OCD probands and their first degree relatives. Thirty variants within the following six genes were genotyped and analyzed using the Family Based Association Test (FBAT): 5HT 1B (5HT1B); 5HT transporter (5HTT, including the 5HTTLPR variant); the glutamate transporter SLC1A1; glutamate receptor ionotropic N-methyl-D-aspartate (NMDA) 1 (GRIN1), GRIN2A and GRIN2B. Phenotypes included OCD diagnosis and lifetime history of principal (target) symptoms within four groups derived from previous factor analyses: 1) Obsessions/checking; 2) Symmetry/ordering; 3) Contamination/cleaning; 4) Hoarding. P values were corrected for multiple comparisons using the Bonferroni method

Results: Promoter polymorphisms of the 5HTTLPR were associated with Contamination/cleaning (p=0.02). Variants in SLC1A1 were associated with Obsessions/checking (p=0.02) and Symmetry/ordering (p=0.004). The heterozygote genotype of a GRIN2B variant was associated with decreased risk for all four subgroups as well as OCD diagnosis (lowest corrected p=0.0006). Conclusions: These results provide further support of an association between OCD and genes in the glutamate and 5HT systems. Although further analysis using larger samples is warranted, this study provides preliminary evidence that using symptom subgroups as endophenotypes may facilitate identification of both vulnerability and protective genes in OCD.

References:

1. Alsobrook J, Leckman J, Goodman W, Rasmussen S, Pauls D: Segregation analysis of obsessive-compulsive disorder using symptom-based factor scores. Am J Med Genet (Neuropsychiatric Genetics) 1999; 88:669-675.
2. Gottesman, II, Gould TD: The endophenotype concept in psychiatry: etymology and strategic intentions. Am J Psychiatry 2003; 160(4):636-45.

NR7 Monday, May 22, 9:00 AM - 10:30 AM

The Association Between Intra-Muscular Haloperidol and Change in the QTc Interval

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Educational Objectives:

This report shows intramuscular injection of haloperidol could increase QTc interval, but these QTc differences were not statistically significant, suggesting haloperidol is relatively safe for cardiac conduction function. Therefore, haloperidol could be a appropriate choice for patients who needs injection of antipsychotics.

Summary:

Objectives

Haloperidol is known to have less adverse effect to heart compare with other antipsychotics. But, some reports suggest that IM or IV haloperidol prolong the QTc interval, associated with an increased risk of torsade de points and of sudden cardiac death. The purpose of this study was to find the adverse effects to heart by a single dose of IM haloperidol on QTc interval.

Methods

The total 23 subjects were hospitalized patients, in Department of Neuropsychiatry, Kuri Hospital, Hanyang Univ. recruited from Jan. to Aug. 2005. The patients with clinically significant cardiac disorder or any abnormality of cardiac conduction disorder in baseline EKG were excluded. The patients medicated 1 hour prior to haloperidol injection or medicated within 8 hour after injection were also excluded. The correlation of the variables such as age, sex, BMI, diagnosis with QTc interval change were estimated.

Results

The mean heart rate-corrected QT interval (QTc interval) increased, from 421.17msec (immediately before injection) to 424.30 msec (after 1 hour) & to 421.22 msec (after 8 hour), but this change was not statistically significant. Age, sex, BMI and diagnosis were not correlated with the QTc prolongation. Any abnormality of cardiac conduction disorder was not detected in EKG either 1 hour or 8 hour after injection.

References:

1. Hatta K, Takahashi T, Nakamura H et al.: The association between intravenous haloperidol and Prolonged QT Interval. J Clin Psychopharmacol 2001; 21:257-261.
2. Harvey AT, Flockhart D, Gorski JC: Intramuscular Haloperidol or Lorazepam and QT Intervals in Schizophrenia. J Clin Pharmacol 2004; 44:1173-1184.

NR8 Monday, May 22, 9:00 AM - 10:30 AM

Comparison of Self, Teacher, and Parent Assessments on Victimization and Bullying in Primary School-Aged Children

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to compare teachers and parents in their abilities to identify which children are bullies and which are victims. The participant should also be able to recognize whether teachers or parents are better able to discriminate between bullies and victims.

Summary:

Objective: To compare teachers' and parents' abilities to accurately identify which children are bullies and which are victims.

Methods: The Peer Interactions in Primary Schools (PIPS) questionnaire was distributed to 95 students in grades 4-6. Each participating student's teacher and parents completed questionnaires to assess their perceptions of bullying or victimization behaviors.

Results: The students who teachers identified as victims had higher scores on the PIPS victim (9.3 ± 6.7 versus 4.8 ± 4.3, p= .02) and bully scale (4.3 ± 3.8 versus 1.6 ± 2.3, p=.01). The students who teachers identified as bullies had higher scores on the PIPS bully (4.8 ± 3.2 versus 1.5 ± 2.2, p<.001) and victim scale (8.8 ± 5.6 versus 4.8 ± 4.5, p=.01). The students who parents identified as victims had significantly higher scores on the PIPS victim scale (7.6 ± 6.1 versus 4.3 ± 3.7, p=.03), but not on the PIPS bully scale. The students who parents identified as bullies had significantly higher scores on PIPS bully scale (4.1 ± 2.8 versus 1.7 ± 2.4, p=.01), but not on the PIPS victim scale.

Conclusions: Both teachers and parents were able to identify bullies and victims. However, the parents had better ability to distinguish bullies from victims.

References:

1. Nansel, T.R., et al., Bullying behaviors among the US youth: prevalence and association with psychosocial adjustment. Jama, 2001. 285(16): p 2094-2100.
2. Espelage DL, ed. Bullying in American Schools: A Social-Ecological Perspective on Prevention and Intervention. 1st ed. Mahwah, New Jersey: Lawrence Erlbaum Associates Inc.;2004.

NR9 Monday, May 22, 9:00 AM - 10:30 AM

Phenomenological Subtypes of Acute Mania: A Factor Analytic Study

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Educational Objectives:

At the conclusion of this session, the participant should be able to understand: (1) The factor structure of the symptoms and signs of Mania (2) The similarity of the factor structure of the symptoms and signs of Mania in different ethnic populations. (3) The clinical significance in distinguishing different subtypes of bipolar disorder and its implications on the selection of treatment modalities.

Summary:

Objectives: There are very few studies of the factor structure of symptoms of mania. All the existing studies have been done in population samples from developed countries. This study replicate the study in a South Asian population sample and establishes inter ethnic validity of the factor structure of symptoms of mania.

Methodology: We rated 168 patients with ICD-10 defined bipolar disorder mania on two scales (1) Mania Rating Scale from Schedule for Affective Disorders and Schizophrenia-change version (2) Scale for Manic States(Cassidy). All the ratings were done by a single physician rater, based on direct interviews of 30-45 minute duration. Principal component factor analysis for each of the scales was carried out using Advanced Statistics package of SPSS. The number of factors was decided based on Eigen values greater than one.

Results: Factor analysis of MRS from SADS-C identified 3 clearly interpretable factors representing irritable paranoid factor, psychomotor acceleration factor, and the factor representing psychosis. Factor analysis of Scale for Manic States (Cassidy) identified 5 clearly interpretable factors representing psychomotor acceleration, increased hedonic function, dysphoric mood, irritable-paranoid features and psychosis. There was no factor representing the severity of illness. Analysis of Cassidy scale identified dysphoric mood, which analysis of MRS filed to identify.

Conclusions: The findings of this study concurs with the findings by Cassidy et al, who also had rated patients with mania using the same instrument, thereby establishing cross-cultural validity of the factor structure of the symptoms and signs of mania. MRS from SADS-C had the limitation of having no variables to capture the dysphoric features, increased socialization and other hedonic factors and hence was not able to identify the factors representing dysphoric mood and increased hedonic function..

References:

1. Cassidy F, Forest K, Murry E, Carroll BJ. A factor analysis of the signs and symptoms of mania.Arch Gen Psychiatry. 1998 Jan;55(1):27-32.
2. Serretti A, Rietschel M, Lattuada E, Krauss H, Held T, Nothen MM, Smeraldi E. Factor analysis of mania. Arch Gen Psychiatry. 1999 Jul;56(7):671-2.

NR10 Monday, May 22, 9:00 AM - 10:30 AM

Subjective Sleep Quality and Dream Anxiety in Patients With BPD

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Educational Objectives:

The present study supports the idea that childhood traumatic events and related dissociative experiences are associated with poor sleep quality and abnormal dream anxiety pattern in patients with BPD.

Summary:

Objective: The aims of this study were to examine the sleep quality, dream anxiety and co-occurrence of nightmare disorder (ND) in a group of patient with BPD and to characterize the influence of childhood traumatic events and dissociative experiences in this association. **Method:** Seventy borderline patients (54 male, 16 female, aged 22.1±3.8) and 70 age- and sex-matched healthy control subjects were assessed by using the SCID-II, Pittsburgh Sleep Quality Index (PSQI), the Van Dream Anxiety Scale (VDAS), Dissociative Experiences Scale (DES), Traumatic Experiences Checklist (TEC) and Hamilton Depression Rating Scale (HRDS) during a 12-month study period. We did not include non-BPD Axis II control groups. **Results:** The main findings were that borderline patients reported a significantly greater proportion of nightmare complaints (52.8%) and had higher VDAS (t=13.8; p<0.001) and PSQI (t=9.8; p<0.001) global scores as compared with controls. The DES scores of borderline subjects were significantly correlated with PSQI (r=0.38; p<0.005) and VDAS (r=0.59; p<0.001) global scores whereas the TEC scores were significantly correlated only with VDAS global scores (r=0.48; p<0.001). There was no significant correlation between depression rates and PSQI and VDAS scores in patients with BPD. Furthermore, borderline patients with ND had significantly higher mean DES (t=8.2; p<0.001), total TEC (t=5.2; p<0.001), global PSQI (t=3.2; p<0.005) and VDAS (t=5.1; p<0.001) scores as compared those without ND. **Conclusions:** The present study supports the idea that childhood traumatic events and related dissociative experiences are associated with poor sleep quality and abnormal dream anxiety pattern in patients with BPD. Borderline patients with ND suffered a greater proportion of sleep problems and reported more frequent child-

hood traumatic events and dissociative experiences according to those without ND. These two disorders (BPD and ND) seem to share, at least partly, the same etiopathogenetic mechanisms.

References:

1. Agargun MY, Kara H, Ozer OA et al.: Nightmares and dissociative experiences. The key role of childhood traumatic events. Psychiatry Clin Neurosci 2003; 57: 139-145.
2. Benson KL, King R, Gordon D, Silva JA, Zarcone VP Jr.: Sleep patterns in borderline personality disorder. J Affect Disord 1990;18:267-73.

NR11 Monday, May 22, 9:00 AM - 10:30 AM

Recent Life Events Preceding Suicide Attempts: Role of Personality Disorders.

Hilario Blasco-Fontecilla III, M.D. *Dr. Rodriguez-Lafora Hospital, Psychiatry, c/ madera 9, 2C, Madrid, 28004, Spain*, Enrique Baca-Garcia, Mercedes Pérez-Rodriguez, Antonio Ceverino-Domínguez, Jose de Leon, Jeronimo Saiz-Ruiz

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that specific recent life events (RLE) may be precipitating factors for suicide in subjects diagnosed with certain personality disorders (PD). For example, narcississtic injuries (e.g. be fired) may precipitate suicide attempts in subjects diagnosed with narcississtic personality disorder.

Summary:

Objective: recent life events (RLE) may be precipitating factors for suicide in subjects diagnosed with a personality disorder (PD). We hypothesized that certain RLE are precipitating factors for suicide in certain PDs.

Method: a sample of 446 suicide attempters seen at the emergency room of two general hospitals in Madrid (Spain) were assessed. The *International Personality Disorders Examination (IPDE)* screening questionnaire was used to diagnose personality disorders. An adjusted cut-off point was used in order to increase specificity and lower the rate of false positives. St Paul Ramsey Life events questionnaire was used to assess RLE.

Results: significant associations were found between *paranoid PD* and "important changes in social activities" (Fisher's Exat Test (FET= 0.029) and "social disputes" (FET= 0.055); *schizoid PD* and "modification in personal habits" (X^2= 6.914; df= 2; p=0.032) and "important personal success" (FET= 0.012); *schyzotypal PD* and "important changes in social activities" (FET= 0.019) and "important change in health or behaviour of a member of the family" (FET= 0.058); *narcissistic PD* and "being fired" (FET= 0.005). Histrionic PD was close to significancy with "problems with political family" (FET= 0.089) and "change of residence" (FET= 0.076). Four PDs -borderline PD, antisocial PD, obsessive-compulsive PD and, evitative PD- had no significant relationship with any RLE.

Conclusions: specific RLE can precipitating factors in certain PDs. They may be assessed carefully when assessing subjects diagnosed with a PD to prevent suicide attempts.

References:

1. Horesh N, Orback I, Gothelf D, Efrati M, Apter A. Comparison of the suicidal behavior of adolescent inpatients with borderline personality disorder and major depression. J Nerv Ment Dis 2003;191(9):582-8.
2. Poulton RG, Andrews G. Personality as a cause of adverse life events. Acta Psychiatr Scand 1992;85,35-38.

NR12 Monday, May 22, 9:00 AM - 10:30 AM

Disposition Toward Humor in Patients With Depression

Anna Bokarius *Cedars-Sinai Medical Center, Psychiatry, 8730 Alden Dr. RmE123, Los Angeles, CA, 90048*, Waguih W. Ishak, M.D., Russell Poland, Ph.D., Mark H. Rapaport, M.D., Vladimir Bokarius, M.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to demonstrate an understanding of the current situation of humor research in psychiatry. The participant would also be able to recognize the relation between humor and depression.

Summary:

The role of humor in the underpinnings, expression and response to the treatment of psychiatric disorders remains unclear. However, the topic recently has been gaining interest in the psychiatric community. Extant, albeit limited, data suggest that humor can reduce stress and anxiety; however, the role humor plays in depressive disorders remains unclear. While it would seem logical that humor and depression are linked, the relationship has not been thoroughly assessed. Accordingly, we decided to first perform a study to assess the relationship between a sense of humor and the severity of depression. Subjects seeking treatment in a large psychiatric outpatient clinic located within a large community mental center filled out the Quick Inventory of Depressive Symptomatology scale and a modified Svebak's Sense-of-Humor Questionnaire. Preliminary results revealed that there were significant negative correlations between the total score the two scales (r=-0.7), as well a negative correlation between depression and perception of humorous messages and emotional expression (r=-0.7). The data indicate that as the severity of depression increases, subjects are less receptive to humor. Further research is needed to determine whether this is a state or trait relationship, whether other demographic variables account for this relationship, or whether humor impacts on response to different treatment modalities.

References:

1. Svebak S: Revised Questionnaire on the Sense of Humor. Scand J Psychol 1974; 15: 329-331.
2. Thorson JA, Powell FC: Depression and Sense of Humor. Psychological Reports 1994; 75: 1473-1474.

NR13 Monday, May 22, 9:00 AM - 10:30 AM

Executive Function and Depression in Patients Hospitalized on aGeneral Medicine Service

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Educational Objectives:

After reviewing this poster the audience will be able to:

1. Recognize the high prevalence of executive function impairment and depression in patients hospitalized on a general medicine service.
2. Understand that executive function impairment is only weakly associated with depression in this sample.
3. Consider other mechanisms for executive impairment in medically ill patients other than co-morbid psychiatric illness.

Summary:

Objective A recent study reports 52% of patients hospitalized on a general medicine service failed at least one executive function

measure within 24 hours of admission. The authors suggest this may be secondary to either the presenting disease processes or to comorbid psychiatric illnesses. This study aims to determine if high depressive symptom burden is associated with executive function impairment in patients hospitalized on a general medicine service.

Method 100 consecutive non-delirious patients hospitalized on a general medicine service were administered the Geriatric Depression Scale (GDS) and the Hamilton Rating Scale for Depression (HAM-D). A blinded co-investigator administered two tasks sensitive to executive function, The Executive Interview (EXIT25) and The Executive Clock Drawing Task (CLOX), and one general cognitive screen, the Mini Mental State Exam (MMSE).

Results 54% scored >8 on the HAM-D and 46% scored >5 on the GDS. 65% failed at least one executive task; 52% scored >15 on the EXIT25 and 35% scored <10 on CLOX1. Poor EXIT25 performance was associated with older age (52.4 years *vs.* 44.7 years, t=3.04, p=0.003) and less education (9.7 years *vs.* 13.1 years, t=4.22, p<0.001). Subjects failing the EXIT25 were more likely to score high on the HAM-D (χ^2=3.90, DF=1, p<0.05) but not the GDS. There were no significant associations between CLOX1 and the depression screens. After adjusting for age, neither the HAM-D nor the GDS contributed significant amounts of variance to either EXIT25 or CLOX1 performance.

Conclusion Executive function was only weakly associated with depression symptom burden. This suggests that the medical illnesses themselves, socio-demographic variables, or other psychiatric co-morbidities may have a greater effect on executive function performance than co-morbid depression.

References:

1. Schillerstrom JE, Horton MS, Earthman BS, Joshi KG, Schillerstrom TL, Velez AM, Royall DR. Prevalence, course, and risk factors for executive impairment in patients hospitalized on a general medicine service. Psychosomatics 2005;46:411-417.
2. Schillerstrom JE, Horton MS, Royall DR: The Impact of Medical Illness on Executive Function. Psychosomatics 2005;46:508-516.

NR14 Monday, May 22, 9:00 AM - 10:30 AM

Tripartite Model of the Mind; An Alternate Explanation to Cognitive Dysmetria in Schizophrenia

Robert G. Bota, M.D. *University of Missouri Kansas City, Psychiatry, 415 n jakson st, americus, GA, 31709*

Educational Objectives:

At the conclusion of this presentation the participant should be able to recognize the concept of "cognitive dysmetria" in which cortical-cerebelar thalmic cortical circuitry shows impairments when compared with individuals without mental illness. The incremental impairment in experiential aspect of perception in patients with psychosis. The cognitive dysmetria can be explained as a "schism" in the interplay of impaired perception and faulty cognition. Our hypothesis suggests a different way of assessing and understanding each individual affected with this illness and ultimately proposes to correct the specific dysfunctions to reduce the decalage between levels of cognition and perception.

Summary:

Background

Schizophrenia is considered to be an illness in which there is a generalized "cognitive dysmetria" in which cortical-cerebelar-thalmic-cortical circuitry shows impairments when compared with individuals without mental illness.

Method

We reviewed the literature pertinent to circuitry abnormalities in schizophrenia. Also, we looked for correlates with severity of illness. Further we focused on described impairments in various domains of insight in schizophrenia.

Results

Form the data gathered we observed that insight into the symptoms is less often impaired than insight into the illness and the consequences of illness. Experiential aspect of perception is obtained from processing primitive awareness through working memory and referenced through the association areas. The reported difficulties for schizophrenia in processing and encoding would lead in time to incremental deteriorations in reality testing. Thinking can be understood as related to perception (impure cognition) and not related to experience (pure cognition, e.g. close systems such as matematics).

We propose that even though are severe dysfunction in each of the presented domains, they occur at different degree of severity. The cognitive dysmetria can be explained as a "schism" in the interplay of impaired perception and faulty cognition.

Discution

Despite the fact that is a vast literature discussing neurological abnormalities in schizophrenia, very limited integrative work was done. Our hypothesis suggests a different way of assessing and understanding each individual affected with this illness and ultimately proposes to correct the specific dysfunctions to reduce the decalage between levels of cognition and perception.

References:

1. Andreasen NC: Schizophrenia: the fundamental questions. Brain Research - Brain Research Reviews 2000; 31(2-3):106-12.
2. Andreasen NC, Paradiso S, O'Leary DS: "Cognitive dysmetria" as an integrative theory of schizophrenia: a dysfunction in cortical-subcortical-cerebellar circuitry? Schizophrenia Bulletin 1998; 24(2):203-18.

NR15 Monday, May 22, 9:00 AM - 10:30 AM

Inflammatory Markers in Sub-Threshold Depression and Major Depression

Marijke A. Bremmer, M.D. *VUMC Medical Center, psychiatry, LASA, Boechhorststraat7, Amsterdam, 1081 BT, The Netherlands*, Aartjan Beekman, Prof. Dr., Dorly Deeg, Prof. Dr., Brenda WJH Penninx, Ph.D., Miranda G. Dik, Ph.D., Witte JG Hoogendijk, Prof. Dr.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand the association between inflammatory processes and depression. Chronic low-grade immune activation might explain the bidirectional relationship between depression and cardiac diseases. New data from the Longitudinal Aging Study Amsterdam will be presented.

Summary:

Background: Although previous studies have found inflammation to be associated with depression, it is still unclear whether this association changes with the severity of the depression. We investigated whether elevated levels of pro-inflammatory cytokines and acute phase proteins are associated with an increased prevalence of subthreshold depression or with major depression in late life, also accounting for actual physical health variables.

Methods: Cross-sectional population-based study of 1285 participants of the Longitudinal Aging Study Amsterdam, aged 65 and over. Plasma concentrations of Interleukin-6 (IL-6), C-reactive protein (CRP) and alpha-1-antichymotrypsin (ACT) were measured. Major depression was established according to criteria of the Diagnostic Statistical Manual (DSM)-third edition. Respondents with clinically relevant depressive complaints that do not

reach DSM criteria were diagnosed as having subthreshold depression.

Results: Elevated levels of CRP, ACT and to a lesser extent IL-6 were associated with a decline in physical health. Subjects with high levels of IL-6 were 2.5 times more likely to have a major depressive episode, independently of co-morbid physical conditions. Only men with elevated levels of ACT were more likely to suffer from subthreshold depression (OR= 2.51 (1.16-5.45)), although they were not more likely to suffer from major depression. Elevated levels of CRP were positively associated with all chronic diseases but not with either subthreshold depression or with major depression.

Conclusions: In older people, the association between depression and pro-inflammatory cytokines or acute phase proteins is different for subjects with subthreshold depression than for those with major depression. A possible relationship with dysregulation of the Hypothalamo-Pituitary-Adrenal axis will be discussed.

References:

1. Capuron L and Miller AH: Cytokines and psychopathology: lessons from interferon alfa. Biol Psychiatry 2004; 56(11):819-824.
2. Kiecolt-Glaser JK et al: Depression and immune function: central pathways to morbidity and mortality. J Psychosom Res 2002; 53:873-876.

NR16 Monday, May 22, 9:00 AM - 10:30 AM

Anger, Gambling, and Substance Use: Is There a Functional Relationship?

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Educational Objectives:

At the conclusion of this presentation, the participant should understand that though dysregulated anger and violence may follow addictive behaviours, addiction behaviours may also serve to regulate dysregulated anger among individuals with concurrent anger and addictions problems.

It is important for clinicians to assess the functional relationships between addictive behaviours and anger.

Summary:

Objective: Recent models of addiction suggest that one pathway to addictive behaviours could occur through affect regulation; research has also looked at emotion's role in problem gambling, suggesting that some pathological gamblers manage unpleasant emotional states by gambling because they lack effective emotion regulation strategies. This study examines the functional relationship between gambling, substance use and anger in a sample of treatment seeking angry, problem gamblers.

Methods: Sixty-two treatment-seeking individuals with concurrent anger and gambling problems- about half also met criteria for a substance use disorder. Inclusion criteria were self-reported anger and pathological gambling, determined by a Canadian Problem Gambling Index (CPGI) score > 7. Participants were 56 men and 6 women, with a mean age of 41.06 years (SD=10.99). Measurements included the State-Trait Anger Expression Inventory (STAXI), CPGI, and Violence and Anger History Interview (VAHI), a structured interview identifying salient angry and violent episodes that have led to serious consequences to the participant and others.

Results: 45.2% of participants reported gambling after angry episodes with serious consequences to themselves. Of these, 61% reported that their anger decreased after gambling. 36% reported using alcohol after becoming angry, and 41% of these participants reported a decrease in anger intensity after drinking. In episodes with serious consequences to others, 30.6% reported they gambled after the anger episode, and 24.2% reported they used alcohol. 68% reported a decrease in anger intensity after gambling, and 47% reported a decrease in anger after drinking.

Conclusions: The findings suggest addiction behaviours serve to regulate anger among individuals with concurrent anger and addictions problems, and provide support for the use of emotion regulation strategies in treating individuals with concurrent anger and addiction problems. Implications for treatment interventions and suggestions for future research will be discussed.

References:

1. Blaszczynski A, Nower L: A pathways model of problem and pathological gambling. Addiction 2002; 97(5):487-499.
2. Baker TB, Piper ME, McCarthy DE, Majeskie MR, Fiore MC: Addiction motivation reformulated: An affective processing model of negative reinforcement. Psychological Review 2004; 111:33-51.

NR17 Monday, May 22, 9:00 AM - 10:30 AM

Adults With Intellectual Disabilities Who Use Hospital Emergency Services for Psychiatric Crises: Client and Caregiver Perspectives

Maaike Canrinus, M.A. *Centre for Addiction & Mental Health, 2527 Yonge St., Toronto, ON, M4P 2H9, Canada*, Yona Lunsky, Ph.D., Jennifer Puddicombe, M.Ed.

Educational Objectives:

At the conclusion of this poster presentation, participants will be able to identify some of the key issues and challenges from the perspective of adults with intellectual disabilities and their caregivers, regarding their experiences visiting the hospital emergency room for a psychiatric crisis.

Summary:

In North America, psychiatric services for adults with intellectual disabilities (ID) were once provided through institutions, but deinstitutionalization has directed these individuals to the generic health care system. Because of a lack of equitable access to mental health care services for this population, adults with ID often visit hospital emergency rooms in the event of a psychiatric crisis. Little is known about these hospital visits, especially from the perspective of adults with ID and their caregivers. Although research has explored the perspective of individuals with ID in terms of their experiences with the emergency room in the case of medical emergencies (Iacono & Davis, 2003), there is no known work exploring hospital visits for psychiatric emergencies. This poster presentation presents the unique perspectives of adults with ID and their caregivers.

Focus groups were held with adults with ID and caregivers of adults with ID, all of whom had experience visiting the emergency room for a psychiatric crisis. Participants addressed issues such as key reasons for emergency room visits, challenges to these visits, and resources needed. Data were analyzed thematically, revealing several consistent themes for both adults with ID and caregivers. These included issues of respect, consent, hospital staff training, difficulties with collaboration between professionals, use of medication, and lack of alternative services. Overall, these findings can be used to better understand how clients and caregivers experience emergency room visits, and may lead to better communication between clients, caregivers, and hospital staff, and ultimately, better experiences and care for adults with ID experiencing psychiatric crises.

References:

1. Iacono T, Davis R: The experiences of people with developmental disability in hospital wards and emergency departments. Res Dev Disabil 2003; 24: 247-264.
2. Sullivan W, Berg JM, Bradley EA, Brooks-Hill RW, Goldfarb CE, Lovering JS, Lunsky Y, Korosy M, Grossman SA, Hutson HR, Anglin D: Enhancing the emergency department outcomes of patients with mental retardation. Ann Emerg Med 2000; 36: 399-400.

NR18 Monday, May 22, 9:00 AM - 10:30 AM

Prevalence of Metabolic Syndrome in VA Bipolar Patients

Jeffrey Cardenas, M.D. *University of California Los Angeles, Psychiatry, 17718 Victory Blvd, Encino, CA, 91316*, Mark A. Frye, M.D., Susan Marusak, M.D., Eric M. Levander, M.D., Jason Chirichigno, M.S., Lori L. Altshuler, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant will have an appreciation for the high prevalence of the metabolic syndrome in patients with bipolar disorder, including prevalence rates for those with and without concurrent treatment for component metabolic syndrome criteria such as diabetes, hypertension, hyperlipidemia. The participant will find that clinically screening for the metabolic syndrome will identify a large proportion of at risk individuals.

Summary:

Background: The metabolic syndrome (MS) is a growing public health problem with 23.7% of the US population meeting criteria for the syndrome.

Objective: To evaluate the prevalence of MS in bipolar subjects treated at the WLAVA Medical Center.

Methods: In this cross sectional prevalence based study, data collected included demographic information, vital signs, and psychotropic drug history. Subjects had a fasting blood draw assessing glucose and lipid profile. Using the National Cholesterol Education Program definition, prevalence rates of MS were calculated with and without concurrent treatment for MS component criteria.

Results: A total of 97 subjects have enrolled. The average body mass indices (Standard Deviation) for the entire cohort, Caucasians, African Americans, Latinos, Asians, and Native Americans were 32 (6.6), 32.6 (7.0), 32.5 (6.4), 29.9 (3.1), 27.9 (3.1), and 26.8 (0) respectively. Of 74 subjects with complete lab data, 50% had MS. 31.1% of subjects were MS positive with concurrent treatment for component criteria, 18.9% were MS positive without concurrent treatment, 14.9% were MS negative with concurrent treatment, and 35.1% were MS negative without concurrent treatment. MS prevalence by current and past psychotropic drug use will be presented.

Conclusions: Bipolar patients have higher rates of MS than the general population. Since MS confers cardiovascular risk and since screening can identify a large proportion of at risk individuals, clinicians should advocate for prevention and treatment of MS.

References:

1. Fagiolini A, Frank E, Scott JA, et al: Metabolic syndrome in bipolar disorder: findings from the Bipolar Disorder Center for Pennsylvanians. Bipolar Disorders 2005; 7: 424-430.
2. Lakka HM, Laaksonen DE, Lakka TA, et al: The Metabolic Syndrome and Total and Cardiovascular Disease Mortality in Middle-Aged Men. Journal of the American Medical Association 2002; 288: 2709-2716.

NR19 Monday, May 22, 9:00 AM - 10:30 AM

Pharmacokinetics of Aripiprazole: Evidence From a Routine Therapeutic Drug Monitoring Service

Ingrid Castberg, M.D. *Brøset Psychiatric Hospital, Department of Forensic Psychiatry, Pb. 1803 Lade, Trondheim, 7440, Norway*, Olav Spigset, Prof. Dr.

Summary:

Introduction: There is limited documentation on the pharmacokinetics of the atypical antipsychotic aripirazole in a naturalistic setting.

Objective: The objective was to investigate the concentration/dose (C/D) ratios of aripiprazole in samples analyzed for routine therapeutic drug monitoring purposes.

Methods: One hundred samples from 81 patients (35 females and 46 males) receiving aripiprazole were collected consecutively. To include each patient only once, a mean value of dose and serum concentration was calculated for those patients who were represented by two or more samples.

All samples were taken 12 to 24 h after ingestion of the last dose, and were analyzed by LC-MS.

Results: The mean dose was 20 mg/d (range 5-37.5 mg/d). Male patients received a slightly higher daily dose than females, with mean values of 22 mg and 18 mg, respectively. The mean age was 34 (range 15-71) years. The mean C/D ratio was 31 (range 3.3-75.6) (nmol/l)/(mg/d). There was no significant gender difference with regard to C/D ratio. There were no trends towards increasing C/D ratios with increasing dose or age. Other drugs were used concomitantly by 58 patients. Comedication with the CYP3A4 inducer carbamazepine caused a 90% decrease in the C/D ratio. Patients comedicated with the CYP2D6 inhibitors levomepromazine or fluoxetine had C/D ratios 30% higher than average. Comedication with valproate caused a 30% decrease in the C/D ratio. Comedication with lithium and lamotrigine did not affect the C/D ratios significantly.

Conclusion: There is a large interindividual variation in the C/D ratio of aripirazole. Comedication with CYP2D6 inhibitors and CYP3A4 inducers affects the serum concentration of aripiprazole.

References:

1. Harrison TS, Perry CM: Aripiprazole. A review of its use in schizophrenia and schizoaffective disorder. Drugs 2004; 64: 1715-1736.
2. DeLeon A. et al: Aripirazole: A comprehensive review of its pharmacology, clinical efficacy, and tolerability. Clin Ther 2004; 26: 649-666.

NR20 Monday, May 22, 9:00 AM - 10:30 AM

The Impact of Behavioural Changes on Quality of Life in Patients With Advanced Alzheimer's Disease

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Educational Objectives:

At the conclusion of this poster presentation, the participants should be aware that improving behavioural symptoms and reducing medication side effects in patients with Alzheimer's disease, even at an advanced disease stage, may measurably improve their quality of life (QOL).

Summary:

Introduction

Behavioural and psychological symptoms of dementia (BPSD) are highly prevalent among those with advanced Alzheimer's disease (AD) and may impact quality of life (QOL). This study exam-

ined whether improvements in BPSD is associated with measurable improvements in QOL for these patients. Moreover, three different QOL measurement scales were compared to assess usefulness in evaluating QOL in this population.

Methods

Longitudinal assessments of QOL, using the Health Utility Index (HUI), the Time-Trade-Off (TTO) scale and the Visual Analogue Scale (VAS), and BPSD, using the Neuropsychiatric Inventory (NPI), were performed in 37 institutionalized patients (23M/14F; age 82.0±6.1) with severe AD (MMSE 3.8±4.6) and BPSD (NPI 27.0±14.8) by means of proxy respondents. The presence and severity of medication side-effects was also scored.

Results

Change in NPI score (range -42 to 40) was significantly correlated with changes in HUI and TTO scores (HUI: r=-.28, p=.02; TTO: r=-.30, p=.02) while no association was found with change in VAS score (p=.21). Also, medication side-effects were found to be negatively associated with TTO score (r=-.29, p=.02). Linear regression analysis indicated that the NPI change (p=.02) and side effects (p=.03) were independent predictors of change in TTO (r=.40; F=5.7; p=.006).

Discussion

Improving behavioural symptoms and decreasing medication side effects are associated with measurable increases in QOL in institutionalized patients with advanced AD. Moreover, this study serves as a preliminary confirmation that the HUI and TTO can detect changes in QOL in this population, and that the VAS is a contrastingly poor scale of choice. While the TTO scale is a less objective measurement tool compared to the HUI, it seems to have an added ability to detect to the impact of medication side effects.

References:

1. Martin-Cook K, Hynan LS, Rice-Koch K, Svetlik DA, Weiner MF: Responsiveness of the Quality of Life in Late-State Dementia Scale to Pyshcotropic Drug Treatment in Late-State Dementia. Dementia and Geriatric Cognitive Disorders 2005; 19:82-85.
2. Mega MS, Cummings JL, Fiorello T and Gornbein J: The spectrum of behavioral changes in Alzheimer's disease. Neurology 1996; 46:130-135.

NR21 Monday, May 22, 9:00 AM - 10:30 AM

Modafinil Augmentation for Fatigue Associated With Fibromyalgia

Susan M. Chlebowski, M.D. *SUNY Upstate, Psychiatry, 713 Harrison St, Syracuse, NY, 13210*, Thomas L. Schwartz, M.D.

Educational Objectives:

At the end of reading this poster, participants will better understand the diagnosis of fibromyalgia and appreciate the level of fatigue these patients experience. Furthermore, participants will be educated about the use of modafinil, in regards to efficacy and tolerability, as a potential treatment.

Summary:

Introduction: Fibromyalgia is a chronic and debilitating illness with a complex biopsychosocial etiology and an even more complex set of available off-label treatments. Fatigue is often associated with fibromyalgia and very few studies exist in regards to treating this symptom. Modafinil is a histamine facilitating agent with effectiveness noted in the treatment of narcolepsy, obstructive apnea and shift work sleep disorder related fatigue. This study focuses on modafnil's ability to treat fatigue associated with fibromyalgia.

Methods: 98 consecutive fibromyalgia patients' charts were systematically reviewed if their medication regimen showed augmentation with modafinil. This retrospective study used an analogue rating scale to determine modafinil's ability to lower fatigue and improve functioning.

Results: Modafinil showed good effectiveness in that fatigue ratings were statistically lowered on average of 26% compared to baseline scores.

Conclusions: In clinical practice, fibromylagia is often treated with a complex regimen of physical therapy, psychotherapy, biofeedback, and polypharmacy. Modafinil seems to be a reasonable addition to this multimodal treatment approach.

References:

1. Rao S, Bennett R: Pharmacological therapies in fibromyalgia. Best Pract & Research Clin Rheum 2003;17(4):611'27.
2. Wolfe F, Smyth H A, Yunus M B, et al.: The American College of Rheumatology 1990 Criteria for the Classification of Fibromyalgia: report of the multi-center criteria committee. Arthritis Rheum 1990;33:160'72.

NR22 Monday, May 22, 9:00 AM - 10:30 AM

The Reliability Study of the Korean Composite International Diagnostic Interview (K-CIDI): Substance Use Disorder Module

Hae Woo Lee, M.D. *Seoul*, Tong Woo Suh, M.P.H., Jin-Pyo Hong, M.D., Bong-Jin Hahm, M.D., Jang-Kyu Kim, M.D., Jae Nam Bae, M.D., Maeng Je Cho, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that our the Korean version-Composite International Diagnostic Interview (K-CIDI), Substance use disorder module reliability fidings are at least as high as those from previous community based studies. K-CIDI, substance use disorder module will be useful epidemiological study tools in evaluating substance use disorders for Koreans.

Summary:

Background: This study aimed to reliability of the K-CIDI (Korean version of the Composite International Diagnostic Interview), substance use disorder module

Method: Substance use patient group under treatment (n=30) were interviewed using the Korean version of CIDI 2.1/DSM-IV. Finding was obtained in institution of Forensic Ministry of Justice in Gongju, Chungcheongnam-do, South Korea. Inter-rater and test-retest Reliability of diagnoses and criteria for nicotine, alcohol, illegal and prescribed drugs were evaluated

Results: Good-to-excellent kappa values for all substance disorders were assessed, with significant kappa values ranging between 0.65 and 1.00(Inter-rater), between 0.70 and 1.00(Test-retest) for drug dependence respectively. There was significant agreement for the assessment of DSM-IV diagnostic criteria for drug (Inhalant) dependence.

Conclusions: Especially, this study was conducted in substance use disorder patient group, our K-CIDI reliability findings are at least as high as those from previous community based studies.

References:

1. Ustun B et al.: WHO Study on the reliability and validity of the alcohol and drug use disorder instruments: overview of methods and results. Drug Alcohol Depend. 1997; 47:161-169.
2. Wittchen HU: Reliability and Validity Studies of the WHO-CIDI: A critical Review. J. Psychiatry Res. 1993; 28: 57-84.

NR23 Monday, May 22, 9:00 AM - 10:30 AM

Psychotropic Medication Prescription Patterns for Children in Publicly Funded Mental Health Clinics in California between 1998-1999

Bowen Chung, M.D. *UCLA Health Services Research, Department of Psychiatry, 10920 Wilshire Blvd, Suite 300, Los Angeles, CA, 90024,* Gang Liu, M.A., Thomas Belin, Ph.D., Penelope Knapp, M.D., Bonnie T. Zima, M.D.

Educational Objectives:

1) To describe psychotropic medication prescription rates among children receiving care for common psychiatric disorders in publicly-funded outpatient clinics in California.

2) To raise awareness of gender and ethnic disparities in acceptable use of psychotropic medication treatment for ADHD and major depression for children.

Summary:

Objective: To describe psychotropic medication prescription rates for children receiving care for ADHD, major depression (MD), and conduct disorder (CD) in publicly-funded outpatient mental health clinics in California and to explore how broad indices of acceptable medication use vary by child and clinic characteristics.

Method: Medical record abstraction using a longitudinal cohort of 813 children ages 6.0-16.9 years with at least 3 months of outpatient care, drawn from a 4,958 patients in 62 mental health clinics in California from August 1, 1998 through May 31, 1999.

Results: Overall 57.6% of children and adolescents with ADHD, MDD, and CD were prescribed any psychotropic medication. Of those with ADHD and MD, 48.6% had been prescribed any stimulant and 57.1% any antidepressant medication, respectively. Among children receiving care for ADHD, younger age was correlated with receiving a stimulant prescription. Among children with MDD, older age was correlated with receiving an antidepressant prescription. There were no ethnic or gender disparities noted in psychotropic prescription patterns.

Conclusion: Psychotropic medication rates in publicly funded mental health clinics for children with documented diagnoses of ADHD and MDD appear to be modest with little more than half of children receiving medication.

References:

1. 1. Zima, B. T., M. S. Hurlburt, et al. (2005). "Quality of publicly-funded outpatient specialty mental health care for common childhood psychiatric disorders in California." J Am Acad Child Adolesc Psychiatry 44(2): 130-44.

2. 2. Zito JM, Safer DJ, dosReis S, Gardner JF, Magder L, Soeken K, Boles M, Lynch F, Riddles MA. Psychotropic practice patterns for youth: a 10 year perspective. Arch Pediatr Adolesc Med. 2003;157:17-25.

NR24 Monday, May 22, 9:00 AM - 10:30 AM

Relationship of Major Depression to Severity of Drug Use, Learned Helplessness, Treatment Readiness, and Coping in Cocaine Dependence

Reynolds C. Clodfelter, Jr., Psy.D. *Southlight, Inc./Duke U., 2809 Highwoods Blvd, Ste 103, Raleigh, NC, 27604,* Kathi Peindl, Ph.D., Paolo Manelli, M.D., Thomas R. Lynch, M. Zach Rosenthal, Ph.D., Ashwin A. Patkar, M.D.

Educational Objectives:

At the conclusion of this presentation, the participants will be able to understand the relationship between major depression and other predictors of cocaine dependence.

Summary:

Objective: Little is known about how predictors of cocaine dependence relate to one another. This presentation will address how major depression that meets DSM-IV criteria is predicted by other factors that are related to cocaine dependence.

Method: 86 cocaine dependent subjects were assessed across 12-weeks of treatment for drug addiction severity and clean urines. At baseline, major depression, learned helplessness, drug addiction severity, treatment readiness, and coping styles were measured. We examined the relationship of major depression to the other predictor variables to determine if any significant associations were present.

Results: 89.5% of the cocaine dependent subjects were black, 58.1% were male, and 32.6% had major depression that met DSM-IV criteria. We examined the relationship of major depression to the other predictors in logistic regression. Addiction severity was the strongest predictor of major depression in this population of cocaine dependent subjects (OR=>40, 95%CI 40-12041; Wald= 9.660; p=0.002). If a subject had low learned helplessness then this factor was protective against major depression (OR=.131, 95%CI=0.035-.487; Wald=9.194, p=0.002). Coping adequacy was related to major depression in that subjects with less coping adequacy were more likely to have major depression (OR=4.278; 95%CI=1.259-14.537; Wald=4.373; p=0.020). Treatment readiness was not significantly related to major depression.

Conclusions: Almost one third of the cocaine dependent subjects had major depression. Good treatment outcomes for cocaine addiction may be affected if the comorbidity of major depression is not addressed. Variables related to cocaine dependence are also strongly associated with major depression and show that treatment should be a multifaceted approach so that major depression, if present is treated in conjunction with cocaine addiction.

References:

1. McDowell, D.M. & Clodfelter, R.C. Depression and Substance Abuse: Considerations of Etiology, Comorbidity, Evaluation, and Treatment. Psychiatric Annals. 2003; 31(4): 244-51.

2. McDowell, D.M., Nunes, E.V., Seracini, A.M., Rothenberg, J., Vosburg, S.K., Ma, G.J., Petkova, E. Desipramine treatment of cocaine-dependent patients with depression: a placebo-controlled trial. Drug Alcohol Depend. 2005 Nov 1;80(2):209-21.

NR25 Monday, May 22, 9:00 AM - 10:30 AM

Adults With Intellectual Disabilities Who Use Hospital Emergency Services for Psychiatric Crises: Hospital Health Care Perspectives.

Sara Cohen-Gelfand, M.S.C. *University of Toronto Medical School, Faculty of Medicine, 3 McAlpine st, toronto, ON, M4R3T5, Canada,* Yona Lunsky, Ph.D., Jennifer Puddicombe, M.Ed.

Educational Objectives:

At the conclusion of this presentation/poster, the participants should be able to understand the challenges and barriers to treating adults with ID in psychiatric crisis. In particular, the participants should be able to recognise the specific issues of the hospital and health care workers. As well, participants should be able to recognize the resources that are needed as well as the possible ways to prevent future emergency department visits and ultimately increase access to and appropriateness of crisis care for this population.

Summary:

The movement of care for adults with Intellectual Disabilities (ID) from instutution to community based has resulted in both positive and negative outcomes for this population. While research has shown that moving away from institutionalized care has im-

proved adaptive skills, decision-making, and behavior management, unfortunately people with ID have also been shown to experience problems with access to and treatment by the health care system. As psychiatric illness is prevalent in individuals with ID, access to psychiatric services is critical. Due to the lack of access to health care, in particular psychiatric services, many individuals with ID present at their local emergency department in psychiatric crisis. Though the experience of adults with ID in the emergency department has been studied in regards to medical issues, the topic has not been examined with regards to psychiatric crisis. In addition, no research has evaluated the experience from the hospital/health care perspective.

This project aims to examine the experience of Adults with ID using emergency hospital services for psychaitric crisis. In particular, this project explores this issue from the perspective of the hospital and health care workers.

Focus groups were conducted with emergency department staff from 6 hospitals in Toronto. Topics discussed included the challenges to treating adults with ID in crisis, resources needed and prevention of future emergency visits. A thematic analysis of the data revealed themes including the need for more resources and crisis support, inadequate hospital staff training, patient behaviour issues, and a lack of interdisciplinary care. It is hoped that the results of this research will increase our understanding of the challenges and barriers to treating adults with ID in crisis. This project aims to ultimately lead to improved access to and treatment in the emergency health care system for adults with ID in psychiatric crisis.

References:

1. Melville CA, Finlayson J, Cooper, SA, Allan L, Rbinson N, Burns E, Martin G, Morrison J. Enhancing primary health care services for adults with intellectual disabilities. J Intellect Disabil Res 2005; 49: 190-198.
2. Iacono T, Davis R: The experience of people with developmental disability in emergency departments and hospital wards. Res Dev Disabil 2003; 24: 247-264.

NR26 Monday, May 22, 9:00 AM - 10:30 AM

The Role of Natural Remedies for the Treatment of Anxiety

Eliza Coleman, B.A. *Cambridge Health Alliance, Psychiatry-Central Street Health Center, 1493 Cambridge St, Cambridge, MA, 02139*, Gustavo D. Kinrys, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand the advantages and disadvantages of the use of natural remedies.

Summary:

Objectives/Background: Anxiety disorders are the most prevalent disorders as a group, with a lifetime prevalence of 24.9% in the general population. As such, they represent a significant burden to society, especially with regard to its associated levels of psychosocial disability, somatic complications, and utilization of health care resources. Despite the effectiveness of currently available treatments for anxiety, many patients (40-65%) remain symptomatic after initial intervention or cannot tolerate the adverse effects commonly associated with conventional treatments. Thus, there remains an outstanding need for efficacious pharmacological agents that are safe, well-tolerated, lead to remission of symptoms, and meet patients' preferences. In this presentation, we will discuss the advantages and disadvantages of the use of natural remedies based on level of evidence, quality of data available, and gaps in the literature.

Method: A systematic review of the literature encompassing the use of natural remedies for the treatment of anxiety disorders.

Results: Despite the growing popularity of natural medications in recent years, there is limited evidence for the effectiveness of many of these natural treatments. A small number of clinical trials with Passiflora Incarnata (Passion Flower), Valerian root, Inositol, St. John's Wort, and Kava-Kava have been conducted. We also identified anecdotal reports for other agents such as SAM-e. Although some studies seem to suggest superiority to placebo and a potential in alleviating anxiety symptoms, therapeutic dosages remain to be clearly determined. Natural remedies seem to be well tolerated and relatively free of adverse effects, with the exception of Kava-Kava.

Conclusions: Natural remedies appear to be safe and effective in the treatment of anxiety. However the evidence available is limited and more research is needed to determine optimal doses. Larger, controlled trials, and head-to-head comparisons with anxiolytics may shed light and help to clarify their role in the psychopharmacological armamentarium.

References:

1. Jorm AF: Effectiveness of Complementary and self-help treatments for anxiety disorders. Medical Journal of Australia 2004; 181 (7): S29-S46.
2. Akhondzadeh S: Passionflower in the treatment of generalized anxiety: a pilot double-blind randomized controlled trial with oxazepam. J Clin Pharm Ther 2001 Oct; 26(5):363-7.

NR27 Monday, May 22, 9:00 AM - 10:30 AM

Efficacy of Group Psychoeducation in Bipolar Disorders: Five-Year Outcome

Francesc Colom, Ph.D. *IDIBAPS, Neuroscience, Villarroel 170, Barcelona, 08036, Spain*, Eduard Vieta, M.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to acknowledge the impact of psychoeducation in the prophylaxis of recurrences in bipolar disorder, with special emphasis on long-term outcome.

Summary:

Background: Group psychoeducation has shown its efficacy on prevention of all sort of bipolar recurrences, including mania/hypomania, mixed episodes and depression (Colom et al., 2003). However, there is a lack of data regarding efficacy in the long-term, as, in the seminal mentioned study efficacy was assessed at 24-month time-cut. Hereby, we introduce the 5-year follow-up results, paying special attention to the comparison of number of episodes.

Methods: One hundred twenty bipolar I and II outpatients in remission (YMRS score <6, Hamilton Depression Rating Sscale-17 score <8) for at least a 6 months period prior to inclusion in the study, who were receiving standard pharmacologicalal treatment, were included in a controlled trial. Subjects were matched for age and sex and randomized to receive, in addition to standard psychiatric care, 21 sessions of group psychoeducation or 21 sessions of nonstructured group meetings. Subjects were assessed monthly during the 21-week treatment period and throughout the 5-year follow-up. For the present study, the main outcome measures were number of episodes and time-to-relapse.

Results: Patients included in the psychoeducation group had fewer relapses (3.88 versus 8.37; t=4.323, p< .001) including all sorts of episodes -mania (.78 versus 1.76; t= 2.822, p<.007), hypomania (.86 versus 1.51; t=2.137, p<.05), mixed phases (.80 versus 1.59; t=2.5, p<.02) or depression(1.38 versus 3.51; t= 3.996, p<.001)-. The survival curve and the Kaplan-Meier survival

analysis suggested a much better outcome for psychoeducated patients.

Discussion; Group psychoeducation is a useful technique for bipolar patients. It prevents bipolar patients from having a high number of relapses. Despite some criticisms regarding the potential relationship between length of the treatment (6 months) and adherence, withdrawal dates are not significantly high in the present study, when compared to other existing psychosocial strategies.

References:

1. 40. Colom F, Vieta E, Martínez-Arán A, Reinares M, Goikolea JM, Benabarre A, Torrent C, Comes M, Corbella B, Parramon G, Corominas J. A randomized trial on the efficacy of group psychoeducation in the prophylaxis of recurrences in bipolar patients wh.
2. 54. Vieta E, Colom F. Psychological interventions in bipolar disorder: From wishful thinking to an evidence-based approach. Acta Psychiatr Scand (Suppl). 2004;422:34-38.

NR28 Monday, May 22, 9:00 AM - 10:30 AM

Assessment of Agitation in Dementia Based on Behavioral Target Symptoms

Kelly M. Cosman, B.S. *University of Rochester, Psychiatry, U of R - PNT / Monroe Community Hospital, 435 E. Henrietta Rd., Rochester, NY, 14620*, Pierre N. Tariot, M.D., Connie J. Holt, M.P.H., Laura J. Jakimovich, M.S., Rosemary Erb, R.N.

Educational Objectives:

At the conclusion of this session, the participant should be able to understand that it may be feasible to rely on the assessment of an individual's behavioral target symptoms of agitation associated with dementia when monitoring response to an intervention, and that this type of assessment may be a suitable alternative to more formal and lengthy psychometric scales in a clinical setting.

Summary:

Objective: Using results from a previous trial (Tariot 1998), we serially assessed individual symptoms of agitation to examine whether this approach could efficiently characterize agitation and measure response to psychotropic medication, as an alternative to relying on comprehensive behavioral rating scales.

Method: 51 nursing home residents with dementia were enrolled in a 6-week placebo-controlled study of carbamazepine for treatment of agitation. All suffered agitation of sufficient severity that their attending physicians recommended treatment with anticonvulsant medication. Primary outcomes were the total Brief Psychiatric Rating Scale (BPRS) and Clinical Global Impression of Change (CGIC). Participants' behavioral target symptoms of agitation were also described; severity was scored from 0(not present) - 3(severe). Presence/absence of target symptoms and mean severity scores between baseline and week 6 were analyzed. Additionally, these changes were compared to changes in mean psychometric scores to detect correlations between the response measurements.

Results: 43 individual target symptoms were identified. The baseline mean number of target symptoms/participant was 6.6(SD 3.1); mean severity scores were 2.2(SD 0.4) and 2.1(SD 0.4) for drug and placebo groups, respectively. Both treatment groups demonstrated reductions in mean symptom severity during the study [drug -0.96(0.6), placebo -0.26(0.5)]; however the difference between groups was statistically significant using Wilcoxon Rank Sum (p-value=0.0005). Regression analysis demonstrated significant correlations between changes in total BPRS and target symptom severity (r=86.4, p-value<0.0001), as well as between CGIC and target symptom severity (r=85.7, p-value<0.0001).

Conclusions: Results suggest that clinical characterization of behavioral target symptoms may be effective in determining response to treatment, at least in patients with dementia and perhaps other diagnoses. This approach may be applicable in usual clinical settings, and could help clinicians systematize their behavioral assessments as well as reduce the time required to adequately examine response to psychotropic medication.

Supported by NIA grant AG-10463.

References:

1. Tariot PN, Erb R, Podgorski CA, Cox C, Patel S, et al: Efficacy and tolerability of carbamazepine for agitation and aggression in dementia. Am J Psychiatry 1998; 155:54-61.
2. Loy R, Tariot PN, Rosenquist K: Alzheimer's disease: behavioral management. In Annual Review of Gerontology and Geriatrics, edited by Oslin D, Katz I, Lawton MP, New York, Springer Publishing Co., 1999, pp136-194.

NR29 Monday, May 22, 9:00 AM - 10:30 AM

Early Worsening During Treatment With Sertraline, Hypericum, or Placebo in MDD

Cristina Cusin, M.D. *Massachusetts General Hospital- Harvard Medical School, Psychiatry, 50 Staniford St, suite 401, Boston, MA, 02114*, Maurizio Fava, M.D., Jonathan E. Alpert, M.D., Andrew A. Nierenberg, M.D., Deborah L. Shear, Faye H. Schwartz, Roy H. Perlis, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the importance of early symptomatic worsening during antidepressant treatment in patients with major depression.

Early worsening of depression severity during treatment is common, is associated with a poorer outcome, but likely not a treatment-specific effect.

Summary:

In a previous study, we found that 30.4% of 694 fluoxetine-treated patients with MDD experienced early symptomatic worsening. To extend this finding and determine its treatment-specificity, we analyzed a second cohort of outpatients with MDD (N = 340) treated with sertraline (mean dosage 75mg ± 21), hypericum (1299mg ± 243) or placebo, in a multicenter, randomized, double-blind study. This clinical trial, previously published, failed to show a difference in response rate between the three arms (2).

In this sample, an "early worsening", defined as an increase of at least 5 points on the Hamilton Depression Rating Scale-17 (HAM-D) compared to the previous visit, was present between week 2 and 6 in 20.2% of patients treated with sertraline, 25,7% of those treated with hypericum and 24.8% of those treated with placebo.

Of those who experienced early worsening, 27.8% subsequently achieved response, defined as 50% decrease in HAM-D, compared to 42.2 % of subjects without worsening ($X2=4.84$, $p<0.05$).Those results confirm that early worsening during treatment is common, associated with poorer outcome, but likely not a treatment-specific effect.

References:

1. Cusin C, Perlis RH, Amsterdam JD, Quitkin F, Reimherr FW, Zajecka J, Beasley CMJ, Fava M: Early symptomatic worsening during treatment with fluoxetine in Major Depression: prevalence and implications, in NCDEU. Boca Raton, FL, 2005.
2. Hypericum Depression Trial Study G: Effect of Hypericum perforatum (St John's wort) in major depressive disorder: a randomized controlled trial. JAMA 2002; 287(14):1807-14.

NR30 Monday, May 22, 9:00 AM - 10:30 AM

Differences in Clinical Presentation of Those Wanting Versus Not Wanting Treatment for Social Anxiety Disorder Secondary to Major Depression

Kristy L. Dalrymple, Ph.D. *Brown Medical School and Rhode Island Hospital, Outpatient Psychiatry, 235 Plain St., Suite 501, Providence, RI, 02905*, Mark Zimmerman, M.D.

Educational Objectives:

Educational Objectives: At the conclusion of this presentation, participants should have a better understanding of the clinical and demographic characteristics of those seeking versus not seeking treatment for Social Anxiety Disorder secondary to Major Depressive Disorder. In addition, participants should have greater knowledge of the clinical implications of these findings.

Summary:

Objective: Social Anxiety Disorder (SAD) is the most common anxiety disorder comorbid with MDD. Up to one third of those with MDD also have SAD. Although most patients with comorbid MDD and SAD desire treatment for both conditions (74%), a small group does not seek treatment for SAD. No study to date has examined the clinical characteristics of those wanting versus not wanting treatment for SAD secondary to MDD. *Method:* The sample consisted of 141 individuals with primary MDD and secondary SAD, with 118 wanting treatment and 23 not wanting treatment for secondary SAD. Participants were recruited as part of the Rhode Island Methods to Improve Diagnostic Assessment and Services (MIDAS) project. All participants completed a structured diagnostic evaluation assessing for Axis I and II disorders, family history, and psychosocial functioning. *Results:* Participants wanting treatment for secondary SAD reported significantly more time out of work and were younger than those not wanting treatment for secondary SAD. There were no significant differences between these two groups on other demographic variables, duration of current depressive episode, number of depressive episodes, current or past social functioning, severity of depression, overall severity of illnesses, or age of onset of either disorder. *Conclusion:* Overall, few significant differences were found between groups in areas related to severity of illness. This suggests that those wanting treatment for secondary SAD are not necessarily more severe than those not wanting treatment for it. However, the fact that those wanting treatment for secondary SAD reported significantly more time out of work than those not wanting treatment for it indicates that impairment in work functioning may be a better predictor of desiring treatment for SAD secondary to MDD.

References:

1. Fava, M. et al: Anxiety disorders in major depression. Comp Psychiatry 2000; 41:97-102.
2. Zimmerman, M., et al.: Clinician recognition of anxiety disorders in depressed outpatients. J.

NR31 Monday, May 22, 9:00 AM - 10:30 AM

Last Neurobiological Findings in Dissociative Disorders

Cristian Damsa *University Hospital, Rue Micheli-du-Crest 24, Geneva, 1211, Switzerland*, Coralie Lazignac, Andrei Cicotti, Melisande Kelley-Puskas, Roberto Pirrotta, Antonio Andreoli

Educational Objectives:

At the conclusion of the presentation, the participant should be able to integrate the most recent neurobiological findings about dissociative disorders, in a clinical context.

Summary:

Summary

Recent neurobiological developments encourage the reevaluation of the relationship between the organic background and the clinical data from patients with dissociative disorders.

Objectives

1. Synthesis of recent neurobiological data about dissociative disorders
2. To search for a link between clinical and neuropsychological data and the neurobiological findings
3. To underline the importance of an integrative (neuro-biological and clinical) approach for dissociative disorders.

Method

An extensive review of the literature (Medline 1980- Nov 2005) was performed on dissociative disorders and of their neurobiological support. All English, French and German publications were retained, furthermore the references of each article were used to identify possible missing studies.

Results

Several studies suggest the involvement of specific areas of the prefrontal cortex (orbito-frontal, medio-frontal and cingular) and the limbic system in the pathogeny of dissociative disorders. Neurobiological and neuro-endocrinological findings are discussed in relation with clinical and neuropsychological data, concerning the regulation of affects and the memory.

Conclusion

The integration of anatomical, biochemical and neuroendocrinological data in the clinical ethiopathogenic models of dissociative disorders seems to be a challenge for neurosciences.

References:

1. Diseth TH. Dissociation in children and adolescents as reaction to trauma--an overview of.
2. Kelley-Puskas M, Cailhol L, D'Agostino V, Chauvet I, Damsa C : Neurobiologie des troubles dissociatifs Annales Médico ' Psychologiques, in press 2005.

NR32 Monday, May 22, 9:00 AM - 10:30 AM

Association Between the C825T Polymorphism of the G-Protein Beta3 Sub-Unit Gene GNB3 and Clinical Improvement With Antipsychotics in Schizophrenia: Meta-Analysis of Four Drug Trials

Vincenzo De Luca *University of Toronto, 250 College St, Toronto, ON, Canada*, Daniel Muller, Steven G. Potkin, Jan Volavka, Jeffrey Lieberman, Herbert Y. Meltzer, James L. Kennedy

Educational Objectives:

At the conclusion of this presentation, the partecipant should be able to discuss the meta-analysis method applied to pharmacogenetics studies of antipsychotics and antidepressants.

Summary:

G-proteins are composed of alpha, beta and gamma subunits. Once activated, these subunits play a major role in the conversion of external receptor activation into intracellular signals. The functional C825T polymorphism of the beta3 subunit gene (GNB3) has recently been shown to modulate antidepressant response, with the T-allele conferring an increased signalling and being associated with favourable antidepressant response. Our goal was to evaluate the collective evidence for an association between the C825T polymorphism and response to antipsychotics. We performed a metanalysis of four different drug-trials. Overall, the four studies showed no indication of an association between allele and antipsychotic response (z=0.22; p=0.826). The results of the four studies are homogeneous (p=0.832) and there is no evidence of publication bias (p=0.374). In conclusion, the C825T polymor-

phism doesn't influence the outcome of the antipsychotic treatment.

References:

1. De Luca V, et al. Pharmacological Research 2005 51: 381-4.
2. Muller DJ et al. Eur Neuropsychopharmacol 2005 15: 525-31.

NR33 Monday, May 22, 9:00 AM - 10:30 AM

Elite Collegiate Athletes: Personality Versus Playing Time as Determinants of Happiness

Katie G. Denny, M.A. *Stanford University, Psychology, 1251 W. McKinley Ave, Apt. D, Sunnyvale, CA, 94086*, Hans Steiner, M.D., Mark Lepper, Ph.D.

Educational Objectives:

At the conclusion of this presentation, participants should have a good feel for the heavy pressure and stressful environment in which student-athletes exist and flourish, and be able to relate the examined environment to their own experiences of working in a fast paced, high stress world. Participants should walk away with an understanding of what environment and personality contribute to how one copes with stressful situations and which factor contributes more significantly to a person's satisfaction with life. Not only will this presentation will present them with a tiny and untraditional slice of the nature versus nurture argument, but it will provide listeners with another medium to think about what leads to true happiness and give them an avenue to think about what aspects of life are truly important for being happy.

Summary:

Objective:

When people are placed in stressful situations, is their happiness governed more by external or internal factors: success or personality? We approach this question through a study of student-athletes at Stanford University, hypothesizing that personality is more enduring than success, and that happiness in athletes remains stable regardless of playing time.

Methods:

We propose that five personality traits may control athletes' happiness: locus of control, optimism/pessimism, theory of intelligence, mindfulness and self-complexity. Data were collected through a standardized questionnaire using previously validated scales for each of these factors as well as for participants' happiness independent of athletics. 140 student-athletes from Stanford were surveyed, including ages from 18-25, men and women, fall team sports (football, men's and women's soccer and basketball, women's volleyball, and field hockey), and all races.

Results:

While playing time (= athletic success) increases from freshmen to seniors there is no corresponding change in happiness (r = .062, $p > 0.21$). Students' personality traits were stable across years. One personality factor, mindfulness, showed a particularly high positive correlation with happiness ($r = .726$, $p < 0.005$). All other personality traits showed similar relationships. These results suggest that the personality characteristics and happiness levels with which an athlete enters college persist without noticeable change throughout their collegiate career, regardless of athletic success (as measured by playing time).

Conclusion:

If, indeed, happiness levels are established prior to college, this finding has important implications for the prediction of how well an athlete will cope with the adversity inevitably encountered playing college sports, and the manner in which therapists approach emotional problems in college athletes. Promotion of particular personality traits (e.g., mindfulness) during adolescence may help buffer student athletes (and others) against the stresses of their college careers.

References:

1. Steiner H: The College Health Related Information Survey (C.H.R.I.S.-73): A screen for college student athletes. Child psychiatry and human development 2003; 34(2), 97-109.
2. Weinberger D: Distress and self-restraint as measures of adjustment across the life span: Confirmatory factor analyses in clinical and nonclinical samples. Psychological assessment 1997; 9(2), 132-135.

NR34 Monday, May 22, 9:00 AM - 10:30 AM

Mood State and Severity as a Predictor of Bipolar Disorder among Antidepressant Non-Responders

Astrid E. Desrosiers, M.D. *Harvard Medical School, Department of Psychiatry, 50 Stanford Street, Suite 580, Boston, MA, 02144*, Robert M.A. Hirschfeld, M.D., Joseph R. Calabrese, M.D., Mark A. Frye, M.D., Thomas R. Thompson, M.D., Michael L. Reed, Ph.D., Gary S. Sachs, M.D.

Educational Objectives:

To identify depression-related symptom predictors of bipolar disorder risk among patients currently in treatment for unipolar depression.

Summary:

Objective: This study explored the relationship between mood state, severity and depression symptoms and bipolar disorder (BPD) risk among currently treated patients with depression.

Method: Psychiatrists from community and private practice clinic settings randomly selected patients with unipolar depression who had one or more prior antidepressant (AD) medication failures. Patients with a diagnosis of BPD, OCD, or schizophrenia were excluded. Patient history and AD use were obtained via record abstraction. A self-administered patient survey collected current depression symptoms via the 20-item Center for Epidemiologic Study-Depression (CESD) scale. BPD risk was assessed via the Mood Disorder Questionnaire (MDQ).

Results: Data were collected from 461 females and 139 males. Stepwise logistic regression identified depressive symptoms associated with a MDQ positive (MDQ+) screen for BPD. For females this included "people were unfriendly" (OR=2.4, p<.002); for males: "felt that people disliked me" (OR=8.8, p<.001), "talked less" (OR=.149, p<.004), "appetite was poor" (OR=3.1, p<.039). Among those with severe CESD depression (n=370), 18.6% screened MDQ+ positive while 29.7% with mild depression (n= 64) screened MDQ+ (chi=4.11, p<.04) suggesting that depression may mask recall for manic symptoms.

Conclusions: Gender specific depressive symptoms may help to identify patients at risk for BPD. Severe depression may mask recall of past mania and manic symptoms. Manic symptom history should be explored during periods of mild or minimal depression to help optimize symptom recall and enhance BPD detection and the likelihood of appropriate treatment.

Research supported by GlaxoSmithKline.

References:

1. Post RM, Leverich GS, Altshuler LL, Frye MA, Suppes TM, Keck PE Jr, McElroy SL, Kupka R, Nolen WA, Grunze H, Walden J. An overview of recent findings of the Stanley Foundation Bipolar Network (Part I). Bipolar Disord. 2003 Oct;5(5):310-9.
2. Mendlowicz MV, Akiskal HS, Kelsoe JR, Rapaport MH, Jean-Louis G, Gillin JC. Temperament in the clinical differentiation of depressed bipolar and unipolar major depressive patients. J Affect Disord. 2005 Feb;84(2-3):219-23.

NR35 Monday, May 22, 9:00 AM - 10:30 AM

Comparison of Quality of Life and Psychosocial Functioning in OCD Versus BDD

Elizabeth R. Didie, Ph.D. *Butler Hospital/ Brown University, Psychiatry, 345 Blackstone Boulevard, Providence, RI, 02906*, Mary Walters, Ed.M., Anthony Pinto, Ph.D., William Menard, B.A., Jane L. Eisen, M.D., Steven A. Rasmussen, M.D., Katharine A. Phillips, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to describe differences and similarities between obsessive compulsive disorder (OCD), body dysmorphic disorder (BDD) and comorbid OCD+BDD on measures of quality of life and psychosocial functioning.

Summary:

OCD (OCD) and BDD are possibly related disorders characterized by markedly poor functioning and quality of life. However, few studies have compared these disorders in these important domains. We compared functioning and quality of life in 210 OCD subjects, 45 BDD subjects, and 40 subjects with comorbid BDD+OCD using reliable and valid measures. OCD subjects and BDD subjects had very poor scores across all measures, with no statistically significant differences between the groups. However, comorbid BDD+OCD subjects had greater impairment than OCD subjects on 11 scales/subscales, which remained significant after controlling for OCD severity. Comorbid BDD+OCD subjects had greater impairment than BDD subjects on 2 scales/subscales, which were no longer significant after controlling for BDD severity. Thus, functioning and quality of life were poor across all three groups, although individuals with comorbid BDD+OCD had greater impairment on a number of measures.

References:

1. Phillips KA, Menard W, Fay C, Pagano M: Psychosocial functioning and quality of life in body dysmorphic disorder. Comp Psych 2005; 46:254-260.
2. Phillips KA, Gunderson CG, Mallya G, McElroy S, Carter W: A comparison study of body dysmorphic disorder and obsessive-compulsive disorder. Jn Clin Psych 1998; 59:568-575.

NR36 Monday, May 22, 9:00 AM - 10:30 AM

Oxcarbacepine in the Ddetoxication in Patients With Polytoxicomania

Aurora Doll, M.D. *Gregorio Marañon Hospital, Psychiatry, aurodoll@hotmail.com, ORTEGA Y GASSETT N8 2A, ALCALA DE HENARES (MADRID), 28803, Spain*, ANA MENA, M.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to treat with oxcarbacepine the withdrawal symptoms (doses, side effects) in the detoxication of patients with polysubstance abuse (alcohol, cocaine, opiates or benzodiacepines). Also can recognize other advantages of this treatment like no dependency risk and the control in the impulsivity levels.

Summary:

Background: new antiepileptics could be an effective treatment of detoxication, without dependency risks. There're some publications about the uses of oxcarbacepine in this area but this study presents two new aspects: the treatment of cocaine craving with oxcarbacepine and patients with polytoxicomania.

Objectives

Evaluate the effectiveness of oxcarbacepine: in the treatment of withdrawal symptoms, reducing the impulsivity and the needs of benzodiazepines in detoxication.

Methods

40 individuals (20 subjects and 20 controls)with polysubstance use from Detoxication Unit in the Gregorio Marañón Hospital. We evaluate the withdrawal symptoms and the impulsivity after 10 days of treatment in the subjects group with: Clinical Institute Withdrawal Assessment (CIWA), Short Opiate Withdrawal Scale (SOWS), Cocaine Craving Questionnaire (CCQ) and the Impulsivity Rating Scale (IRS). And evaluate the severity of the symptons and their recovery due to therapeutical interventions with the Clinical Global Impression (CGI)

Results

The mean dose of benzodiazepines was 24,25 mg (DS 20,48) in oxcarbacepine group versus 49,01 mg (DS 17,80) in non-oxcarbacepine group, we compared them and there was a significance difference p<0,05.The mean score of following scales was: CIWA 6,22 (DS 3,3), SOWS 8,68 (DS 1,5), CCQ 146,75 (DS 26,52). All of them are low levels of symptoms In IRS, the mean was 4,3 (DS 2,4) that means low levels of impulsivity. In the CGI all the patients of the subjects group were considered severe and 19 of the 20 had an important improvement.

Conclusions: oxcarbacepine was effective for the control of withdrawal symptoms, impulsivity and reduced the needed of use benzodiazepines.

References:

1. Gentry JR, Hill C, Malcolm R. New anticonvulsants: a review of applications for the management of substance abuse disorders. Ann Clin Psychiatry. 2002 Dec;14(4):233-45.
2. Myrick H., Henderson S., Brady K., Malcolm R. Gabapentin in the treatment of cocaine dependence. A case series. J Clin Psychiatry 2001; 62:19-23.

NR37 Monday, May 22, 9:00 AM - 10:30 AM

Differences in Sustained Attention in Methadone Maintained and Abstinent Opiate Dependent Subjects: PET Neuroimaging Study

Daniel Eisenberg, M.D. *Beth Israel Medical Center, Department of Psychiatry, First Avenue at 16th Street, #6KY2, New York City, NY, 10003*, James Prosser, M.D., John A. Matochik, Ph.D., Lisa J. Cohen, Ph.D., Igor I. Galynker, M.D.

Educational Objectives:

Educational Objectives: At the conclusion of the presentation, participants should be able to appreciate differences in attentional processes and regional variations in cerebral glucose metabolism between methadone maintained and abstinent opiate dependent subjects.

Summary:

Objective: Opiate-dependent individuals demonstrate cognitive deficits that may impair their ability to engage in treatment (Darke, 2000). Previous neuroimaging research has identified large regions of the anterior cingulate, right frontal cortex, and left parietal cortex, which are activated during an auditory continuous performance task (CPT) (Benedict, 1998). Few studies have examined how opiate addiction affects attentional processing. We sought to examine whether CPT performance and its metabolic correlates in the brain vary with methadone maintenance or protracted abstinence from opiates.

Method: Thirteen healthy adults, nine former opiate addicts receiving methadone maintenance treatment and twelve former opiate addicts who previously received methadone maintenance and are currently in protracted abstinence underwent neuroimaging using 5-fluorodeoxyglucose PET while performing an auditory CPT.

Results: Methadone maintained subjects had a statistically significant reduction in CPT percentage complete compared to former

addicts in protracted abstinence and healthy controls. There was no significant difference between controls and abstinent subjects with respect to CPT performance. CPT performance covaried positively with regional glucose metabolism in clusters in the left auditory cortex and bilateral thalamus in controls, in no regions in the protracted abstinent group, but in the right mesial occipital, bilateral parietal, bilateral prefrontal, and right posterior parietal cortices in methadone maintained subjects.

Conclusion: Methadone maintained individuals and not abstinent former heroin users demonstrate worse sustained attention than healthy controls. Cortical activity is associated with task performance in methadone maintained individuals in much more widespread cortical areas, suggesting the possibility that methadone patients may require increased activity throughout a diffuse cerebral network in order to sustain attention successfully.

References:

1. Darke S, Sims J, McDonald S, Wickes W: Cognitive impairment among methadone maintenance patients. Addiction 2000; 95:687-95.

2. Benedict RH, Lockwood AH, Shucard JL, Shucard DW, Wack D, Murphy BW: Functional neuroimaging of attention in the auditory modality. Neuroreport 1998; 9:121-6.

NR38 Monday, May 22, 9:00 AM - 10:30 AM

Temperament and Character Inventory and Depression After Diagnosis of Breast Cancer

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize own temperemant and character.

Summary:

Objectives: First, the objective of the present study was to investigate the differences of temperament and character traits between depression group(n=27) and non-depression group(n=29) in Breast Cancer patients. Second, it was to explore the effect of those factors on depression in breast cancer patients.

Methods: Of the 115 subjects, 56 individuals were completed the 17-item Hamilton Depression Rating Scale(HDRS-17) with clinician and Korean version of Temperament and Character Inventory(TCI).

Results: depression group showed significantly higher 'Harm avoidance', and lower Self-directedness' score as compared to non-depression group. The stepwise linear regression analysis showed 'HA1(worry and pessimism)' was the only significant predicting variable for depression.

Conclusion: These data suggest that temperaments and characters should be considered in studies investigating depression from acute stressful events.

References:

1. Grucza RA, Przybeck TR, Spitznagel EL, Cloninger CR. Personality and depressive symptoms: a multi-dimensional analysis. J Affect Disord 2003; 74: 123-30.

2. Richter J, Polak T, Eisemann M. Depressive mood and personality in terms of temperament and character among the normal population and depressive inpatients. Personality and Individual Differeces 2003; 35: 917-927.

NR39 Monday, May 22, 9:00 AM - 10:30 AM

Bicultural Identity Among Economical Migrants: Preliminary Validation of the Geneva Biculturality Questionnaire

Ariel Eytan, M.D. *Geneva University Hospitals, Psychiatry, 2 Ch. Petit-Bel-Air, Geneva, 1225, Switzerland*, Nuria Jene-Petschen, M.D., Marianne Gex-Fabry, M.S.C.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand how the Geneva Biculturality Questionnaire was constructed and validated. Relevant cultural identity items for a multi-ethnic population of economical immigrants living in Switzerland will be presented and discussed.

Summary:

Objective: Acculturation is one of the determinants of mental health among immigrants. Measuring adaptation to the host culture is insufficient, since immigrants will develop various degrees of bi- or multicultural identity. The objective of the present study was to validate a bicultural scale to be used among economical immigrants living in Switzerland. *Method:* A 24 item instrument was designed. The validation study included 93 immigrant adults from three south European countries (Italy, Portugal and Spain), who lived in Geneva. Thirty-eight patients were recruited in an outpatient program for alcohol-related problems and 55 participants were hospital employees. *Results:* The questionnaire was rated as easy or rather easy by 97.8% of participants. Median time to complete it was 5 minutes. The subscales related to culture of origin and host culture displayed adequate internal consistency (Cronbach's alpha 0.77 and 0.73 respectively). Principal component analysis supported the concept of a two-dimensional model, with levels of involvement in culture of origin and host culture independent from each other. Testing logical hypotheses in accordance with literature data provided support to construct validity. The instrument allowed discriminating between patients and healthy subjects, with scores for Swiss culture significantly higher among hospital workers. Younger age at arrival in host country and longer stay were significantly associated with higher score on the Swiss subscale. Longer stay in host country and less frequent return to country of origin were associated with lower score for culture of origin. Biculturality indices were derived in order to identify individuals who are highly immersed in both cultures. *Conclusions*: The proposed instrument allows assessing the bicultural identity of Italian, Portuguese and Spanish economical migrants in Switzerland. Preliminary results prompt to further validation in various and larger patient populations.

References:

1. Cortes DE, Rogler LH et al. : Biculturality among Puerto Rican adults in the United States. Am J Community Psychol 1994; 22: 707-21.

2. Ryder AG, Alden LE et al.: Is acculturation unidimensional or bidimensional? A head-to-head comparison in the prediction of personality, self-identity, and adjustment. J Pers Soc Psychol 2000 ; 79: 49-65.

NR40 Monday, May 22, 9:00 AM - 10:30 AM

Imaging White Matter in Eight Year Old Children With Depressive Symptoms: Diffusion Tensor Imaging Study

Cherine Fahim, Ph.D. *The Montreal Neurological Institute, Department of Neurology and Neurosurgery, 3801 University, Montreal, PQ, H3A 2B4, Canada*, Daniel Perusse, Ph.D., Boualem Mensour, Ph.D., Gille Beaudouin, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the presenter points to the potential benefit of early (during childhood) neuroimaging screening of the white matter

(WM) using diffusion tensor imaging based on symptom tendencies towards depression. In our case, we used children with depressive symptoms (depression tendency DT), however, they did not yet develop the disease. We propose that whole brain WM abnormalities have their effect by disrupting connections between cortical and subcortical regions involved in mood regulation early during childhood in some children DT. Further disruption of these circuits may result in the actual diagnosis of depression. Potentially, if enough connecting WM tracts are impaired, depression may become treatment refractory. It is possible that these findings represent measurable functional changes that can predispose an individual to develop the cognitive and emotional changes that occur in depression. In summary, early investigation of WM abnormalities in certain mental disorders may have clinical utility in early diagnosis,

treatment response monitoring, or the development of new treatments.

Summary:

Objective: Using diffusion tensor imaging, we investigated white matter (WM) in 8 years old children with depressive symptoms (DS) in an attempt to overcome limitations of previous studies on depression (e.g., most studies investigates eledely/adult patients, after the onset of depression and brain changes due to medications/other treatments). **Methods:** Depressive symptoms were evaluated using the Dominic Interactive (Valla et al., 2000). **Results:** We found significant values of lower fractional anisotropy (FA an index of the presence and coherence of oriented WM structures) values in the right (R) hippocampus, R orbital frontal, R medial frontal, left lateral prefrontal, R rostral anterior cingulate, R subgenual cingulate gyri and R anterior thalamus in the DS group (n=10, 3 girls and 7 boys). There were no areas of significantly higher FA in DS compared with NC (n=10, 4 girls and 6 boys). **Conclusion:** These findings suggest that children with DS may have a disruption in the structural integrity of WM in these regions early before the actual onset of the disease. These structural abnormalities may contribute to the tendencies towards depression, which could later result in the actual onset of depression.

References:

1. Seminowicz DA, Mayberg HS, McIntosh AR, Goldapple K, Kennedy S, Segal Z, et al: Limbic-frontal circuitry in major depression: a path modeling metanalysis. Neuroimage 2004;22(1):409-18.
2. Drevets WC, Ongur D, Price JL: Neuroimaging abnormalities in the subgenual prefrontal cortex: implications for the pathophysiology of familial mood disorders. Mol Psychiatry 1998;3(3):220-6, 190-1.

NR41 Monday, May 22, 9:00 AM - 10:30 AM

Medical and Psychiatric History: Predictors of Bipolar Disorder Risk in Patients Treated for Unipolar Depression

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Educational Objectives:

To identify co-morbid conditions, family health history and suicide as potential predictors of bipolar disorder risk among patients currently in treatment for unipolar depression.

Summary:

Objective: This study evaluated patient and family health history data for patients with depression and assessed risk for bipolar disorder (BPD).

Method: Psychiatrists from community and private practice clinic settings randomly selected patients with unipolar depression who had one or more prior antidepressant (AD) medication failures. Patient history and AD use were obtained via record abstraction. A patient survey collected demographics, self-reported "conditions you have been diagnosed with" and "conditions a blood relative (parent, brother, sister, child) may have been diagnosed with", as well as history of suicide thoughts and attempts. BPD risk was obtained via Mood Disorder Questionnaire (MDQ).

Results: Data were collected for 602 patients. Predictors of MDQ+ BPD risk were identified with logistic regression controlling for patient age and gender. For patient reports about their own health problems this analysis yielded: anxiety/bad nerves (OR= 2.7, p<.001), asthma (OR=1.9, p<.009), eating disorder (OR=2.8, p<.001) and OCD (OR=2.3, p< .009). For patients reporting about blood relatives this analysis yielded: arthritis (OR=2.3, p<.001), bipolar disorder (OR=2.0, p<.003), cholesterol problems (OR= 1.8, p<.007) and high blood pressure (OR=.001, p<.001). Suicide thoughts (OR=2.1, p<.003) and suicide attempts (OR=1.9, p<.005) were also associated with MDQ+ BPD risk.

Conclusions: Medical and psychiatric co-morbidities may have treatment implications in depressed patients refractory to standard antidepressant treatments by predicting the likelihood of bipolar disorder.

Research supported by GlaxoSmithKline.

References:

1. Gaudiano BA, Miller IW. Anxiety disorder comobidity in Bipolar I Disorder: relationship to depression severity and treatment outcome. Depress Anxiety. 2005;21(2):71-7.
2. Vieta E, Colom F, Corbella B, et al. Clinical correlates of psychiatric comorbidity in bipolar I patients. Bipolar Disord. 2001;3:253-258.

NR42 Monday, May 22, 9:00 AM - 10:30 AM

Reductions in Behavioral Avoidance During Acute Fluoxetine Treatment for Depression

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the potential impact of antidepressant medication on behavioral avoidance and consider its implication in treatment planning.

Summary:

Objective: Avoidance of upsetting stimuli has been established as a central maintaining feature of anxiety disorders. More recently, various markers of avoidance have been shown to be elevated among individuals with depression and predictive of worse response to treatment for depression and slower remission from MDD. In the present study, we investigated the time course of improvement in behavioral avoidance during acute fluoxetine treatment in patients with MDD.

Method: Five hundred seventy subjects with MDD were treated with fluoxetine for 12 weeks [target dosages: 10 mg daily (week 1), 20 mg (weeks 2-4), 40 mg (weeks 4-8), and 60 mg (weeks 5-12)]. Behavioral avoidance was assessed at baseline and weeks 4, 8, and 12 using a single item from the Hopkins Symptom Check-

list (SCL-90; Derogatis et al., 1974; Item 50). Depression severity was assessed at these time points with the 17-item Hamilton Rating Scale for Depression (Hamilton, 1960). In a hierarchical linear modeling framework, a random slopes repeated measures model (i.e., a growth curve model) was used to assess change in behavioral avoidance over the course of treatment.

Results: Behavioral avoidance decreased significantly during the 12-week treatment ($p < .001$). This result remained significant when depression symptoms, measured during the same visit as the avoidance assessments, were included in the model.

Conclusions: Acute treatment with fluoxetine may help to decrease behavioral avoidance among individuals with depression. This result is independent of concurrent decreases in depression severity. This finding has implications for combined treatments suggesting that pharmacotherapy may help patients prepare to re-engage with valued goals and pleasant activities, a clinical target of the behavioral activation component of cognitive-behavior therapy.

References:

1. Papakostas, GI, Petersen TJ, Farabaugh AH, Murakami JL, Pava JA, Alpert JE, Fava, M, Nierenberg, AA: Psychiatric comorbidity as a predictor of clinical response to nortriptyline in treatment-resistant major depressive disorder. Journal of Clinical Ps.
2. Öngür D, Farabaugh A, Iosifescu, DV, Perils R, Fava M: Tridimensional Personality Questionnaire Factors in Major Depressive Disorder: Relationship to Anxiety Disorder Comorbidity and Age of Onset.Psychotherapy and Psychosomatics 2005; 74: 173-178.

NR43 Monday, May 22, 9:00 AM - 10:30 AM

Continuous Emotional Task Selectively Activates Both Left and Right Amygdala: ^{18}FDG-PET Study

Emilio Fernandez-Egea, M.D. *Hospital Clinic, Servei Psiquiatria (G096) - Programa Esquizofrenia Clinic (PEC), C/Villarroel 170, Barcelona, 08036, Spain*, Eduard Parellada, M.D., Francisco Lomeña, M.D., Javier Pavia, Carles Falcon, Anna Mane, M.D., Miguel Bernardo, Prof. Dr.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand the value of FDG-PET for facial emotion recognition studies

Summary:

Background: Human amygdala plays a key role on affect and emotion circuitry. Amygdalar activation has been consistently shown during facial emotion recognition studies. Most of the amygdalar neuroactivation research have been done with fast temporal resolution techniques, such as fMRI, PET H_20^{15} or Magnetoencephalographic, in part due to habituation phenomena (nervous phenomena that allows to exclude irrelevant and repetitive stimuli). In contrast, some researchers suggest that ^{18}FDG-PET could assess better global emotionality over particular emotion. **Objective:** To study amigdalar response during facial emotion recognition tasks with ^{18}FDG-PET technique. **Methods:** Seven right-handed healthy subjects performed two scans on different days, with both emotional (ET) and control task (CT). Each task consisted on 300 pictures, 3.5 seconds per picture for a total time of 20 minutes of continuous task. ET evaluated sadness and happiness of men and women pictures while CT displayed men and women neutral faces. SPM2 analyses subtracting CT from ET images were performed (amygdalar region of interest - ROI). Time responses and Extended Release rors were also recorded. **Results:** Both left and right amigdalar activation was observed, greater in left ($t = 6.31$; $p < 0.001$) than right ($t = 2.06$; $p = 0.042$) amygdala. There was no different correct answer index between EC and CT (97.5% versus 98,4%; $X^2 = 4.237$; $p = 0.051$) . ET time response was greater than CT (846.54 *vs.* 618.76 miliseconds; $t = 23.89$; $p < 0.001$). **Conclutions:** Lack of amygdala habituation was observed. Continuous emotional task selectively activates both left and right amygdala and it can be assessed with ^{18}FDG-PET technique.

References:

1. Gur RC et al: Brain activation during facial emotion processing. Neuroimage 2002; 16:651-662.
2. Zald DH: The human amygdala and the emotional evaluation of sensory stimuli. Brain Res. Brain Res. Rev 2003; 41:88-123.

NR44 Monday, May 22, 9:00 AM - 10:30 AM

Pathological Aging of Attention in Huntington, Alzheimer, and Normal Subjects

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Educational Objectives:

To help understanding the consequences of attention disorders on aging and dementia

Summary:

Objective.

Recent models have proposed that attention includes exogenous and endogenous attention as separate components. Exogenous attention, defined as automatic, involuntary and unaffected by memory load, is directed by external stimulation. Endogenous attention, defined as voluntary, executive and affected by memory load, is directed by voluntary acts.

Method.

Three studies (2 of our own) were designed to examine if the decline in these two components of attention was similar in normal aging and neurodegenerative diseases. Standardized tests derived from Posner's model of visuospatial attention were administered to normal healthy elderly subjects (n=13), patients with Huntington's disease (HD) (n = 17) and Alzheimer's disease (AD) (n = 15), and matched control subjects (n = 57).

Results.

In healthy elderly subjects, both exogenous and endogenous attention were found to decline, within normal limits, and the decline was more pronounced in endogenous attention in situations of perceptual conflict. In AD, there was a significant decline in both attention components, whereas in HD, voluntary components were markedly impaired, but automatic components preserved.

Conclusions.

The results are consistent with the hypothesis that neuronal networks for attention are differentially vulnerable to the effects of normal aging and neurodegenerative diseases, depending on their cortical or subcortical origins.

References:

1. Flashman LA: Disorders of awareness in neuropsychiatric syndromes: an update. Curr Psychiatry Rep 2002; 4(5):346-53.
2. Foster JK: Selective attention in Alzheimer's disease. Front Biosci 2001; 1 (6): 135-53.

NR45 Monday, May 22, 9:00 AM - 10:30 AM

Antidepressant-Related Relapse in Bipolar Disorder

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Atlanta, GA, 30322, Benjamin Zablotsky, B.A., David J. Borrelli, Michael Ostacher, Rif S. El-Mallakh, M.D., Claudia F. Baldassano, M.D., S. Nassir Ghaemi, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to determine if antidepressant discontinuation leads to increased risk of relapse in bipolar disorder.

Summary:

References:

1. Altshuler L, Suppes T, Black D, Nolen WA, Keck PE, Jr., Frye MA, McElroy S, Kupka R, Grunze H, Walden J, Leverich G, Denicoff K, Luckenbaugh D, Post R: Impact of antidepressant discontinuation after acute bipolar depression remission on rates of depressive relapse at 1-year follow-up. Am J Psychiatry; 2003; 160(7):1252-62

2. Prien RF, Kupfer DJ, Mansky PA, Small JG, Tuason VB, Voss CB, Johnson WE: Drug therapy in the prevention of recurrences in unipolar and bipolar affective disorders: A report of the NIMH Collaborative Study Group comparing lithium carbonate, imipramine, and a lithium carbonate-imipramine combination. Arch Gen Psychiatry; 1984; 41:1096-1104.

ABSTRACT

Objective: Some studies suggest that antidepressant continuation improves outcomes following recovery from bipolar depression. We report interim data from the first randomized controlled trial to assess antidepressant discontinuation with new generation agents in bipolar disorder.

Method: Subjects recovered from a major depressive episode for 2 months (on mood stabilizer plus antidepressant), were openly randomized to either continue (LT; n=30) or discontinue (ST; n= 33) antidepressants, with at least 1 year follow-up. A questionnaire (rated -2 to +2 each) measuring patient opinion on antidepressant use was administered prior to randomization.

Results: A partial analysis was conducted (n=66). In an unadjusted survival analysis of time to first mood episode the ST group seemed more likely to relapse (HR=1.77, 95% CI [1.45, 2.15]). After adjusting imbalanced covariates, the ST group was less likely to relapse (HR=0.13, 95% CI [0.08, 0.22]). Apparent superiority of antidepressant continuation in univariate analysis may reflect confounding bias. Patient expectation (attitude) was a major confound in regression analysis.

Conclusions: Observational evidence of antidepressant benefit is likely due to confounding bias. Randomization and adjustment for confounders demonstrate *increased* depressive relapse with antidepressant continuation.

Funding Source: Supported by NIMH grant MH-64189-03

References:

1. Altshuler L, Suppes T, Black D, Nolen WA, Keck PE, Jr., Frye MA, McElroy S, Kupka R, Grunze H, Walden J, Leverich G, Denicoff K, Luckenbaugh D, Post R: Impact of antidepressant discontinuation after acute bipolar depression remission on rates of depr.

2. 2. Prien RF, Kupfer DJ, Mansky PA, Small JG, Tuason VB, Voss CB, Johnson WE: Drug therapy in the prevention of recurrences in unipolar and bipolar affective disorders: A report of the NIMH Collaborative Study Group comparing lithium carbonate, imipra.

NR46 Monday, May 22, 9:00 AM - 10:30 AM

Intramuscular Ziprasidone for Acute Agitation in Children and Adolescents: Retrospective Chart Review.

Jacob J. Forrester, M.D. *University of Cincinnati, Psychiatry, 3864 Isabella Avenue, Cincinnati, OH, 45209-2127*, Drew H. Barzman, M.D., Stephen M. Montgomery, Nicole B. Clark, Melissa P. DelBello, M.D.

Educational Objectives:

Educational Objective:

1. To determine the effectiveness of intramuscular ziprasidone in the management of acute agitation in children and adolescents.
2. To determine the safety of intramuscular ziprasidone in the management of acute agitation in children and adolescents.

Summary:

Abstract: Introduction: Intramuscular ziprasidone has become a widely used clinical tool to control acute episodes of agitation. However, there is a paucity of data regarding the effectiveness and tolerability of this medication in children and adolescents. METHOD: A retrospective chart review was conducted of children and adolescents admitted to Cincinnati Children's Hospital Medical Center (CCHMC) psychiatric units between January 1, 2003 and June 31, 2005. Subjects who had received intramuscular (IM) ziprasidone were identified and their age, gender, race and dosage received were recorded. Medical records were reviewed to determine the effectiveness and tolerability of IM ziprasidone. Results: Fifty-six youth received IM ziprasidone. Seventeen patients received more than one administration over the course of their hospitalization. Sixty-six injections of 20 mg and 17 injections of 10 mg were administered. Sixty-four percent of injections were given to male patients. The average age of patients receiving an injection was 12.8 years old (range 5-18 years old). Six injections were given to preschool age children (3-7 years old), 8 injections given to school age (8-11 years old), and 59 injections were given to adolescents (> 12 years old). Forty-one patients (49%) receiving injections were African American, thirty-nine (47%) were Caucasian and three (4%) were bi-racial. Re-administration within 4 hours for continued agitation was required only once, after a dose of 10 mg. Four subjects had mild adverse events including generalized myalgia, back pain, confusion, and a nose bleed. Conclusion: These preliminary results suggest that intramuscular ziprasidone was well tolerated for the treatment of acute agitation in children and adolescents. Additional effectiveness analyses will also be presented.

References:

1. Staller JA: Intramuscular ziprasidone in youth: a retrospective chart review.
2. Hazaray E, Ehret J, Posey DJ, Petti TA, McDougle CJ: Intramuscular ziprasidone for acute agitation in adolescents. J Child Adolesc Psychopharmacol. 2004 Fall;14(3):464-70.

NR47 Monday, May 22, 9:00 AM - 10:30 AM

Metabolic Syndrome and the Risk of Coronary Heart Disease in Patients Treated With Second Generation Antipsychotic Drugs

Anne M. Frederickson, M.D. *Zucker Hillside Hospital, Psychiatry, Zucker Hillside Hospital, Glen Oaks, NY, 11004*, Christoph U. Correll, M.D., John M. Kane, M.D., Peter Manu, M.D.

Educational Objectives:

At the concluxion of the presentation the participant should be able to diagnose metabolic syndrome and recognize the fact that the syndrome doubles the 10-year risk of coronary heart disease events (angina, myocardial infarction and sudden cardiac death) in pateints treated with second generation antipsychotic drugs.

Summary:

Objective: To examine the relationship between presence of metabolic syndrome and the risk of coronary heart disease (CHD) events (angina pectoris, myocardial infarction and sudden cardiac

death) in patients treated with second-generation antipsychotic medications.

Methods: 367 adults treated with second-generation antipsychotics randomly selected from consecutive psychiatric admissions to a single hospital underwent assessments evaluating the presence of metabolic syndrome. The 10-year risk of CHD events was calculated according to the Framingham scoring system for age, smoking, total cholesterol, HDL-cholesterol, blood pressure and history of diabetes, and compared in patients with and without the metabolic syndrome.

Results: Metabolic syndrome, present in 137 (37.3%) patients, was associated with a significantly greater age- and ethnicity-adjusted 10-year risk of CHD events, i.e., 11.5% versus 5.3% for men (odds ratio: 2.18, 95% CI: 1.88-2.48, p<0.0001) and 4.5% versus 2.3% for women (odds ratio: 1.94, 95% CI: 1.65-2.23, p=0.0005). The increased risk of CHD events in patients with metabolic syndrome remained significant after the exclusion of diabetic patients. In a logistic regression analysis of variables independent of the Framingham scoring system, triglyceride levels (p<0.0001), waist circumference (p=0.035) and Caucasian race (p=0.047) were significantly associated with the 10-year risk of CHD events (p<0.0001).

Conclusions: These data confirm the high prevalence of metabolic syndrome in patients receiving second-generation antipsychotics, indicate that metabolic syndrome doubles the 10-year risk of CHD events in this population and emphasize the importance of the "hypertriglyceridemic waist" for the identification of psychiatric patients at high risk of CHD.

References:

1. Cohn T, Prud'homme D, Streiner D, et al. Characterizing coronary heart disease risk in chronic schizophrenia: High prevalence of the metabolic syndrome. Can J Psychiatry 2004;49:753-760.
2. Goff DC, Sullivan LM, McEvoy JP, et al. A comparison of ten-year cardiac risk estimates in schizophrenia patients from the CATIE study and matched controls. Schizophrenia Research 2005;80:45-53.

NR48 Monday, May 22, 9:00 AM - 10:30 AM

There Are No Associations Between Immunoglobuline-E and Anxiety and Depression in the Adult General Female Population

Marianne K. Fremstad, M.D. *National University for Technology and Science, Norway, The Institute of Neuromedicine, Borgundvegen 227 B, Aalesund, 6008, Norway*, Arnstein Mykletun, M.A.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to reevaluate previous hypotheses concerning etiological factors in the association between anxiety/depression and eczema, asthma and rhinitis.The finding of no association between anxiety/depression and IgE must encourage development of new hypotheses for the biological link underlying the association between asthma, rhinitis, eczema and anxiety and depression.

Summary:

Objective

There are multiple reports of increased prevalence of anxiety and depression in patients with asthma, eczema and rhinitis. Suggested biological mechanisms underlying these associations most commonly involve IgE. However, the association between anxiety/depression and IgE has hardly been studied, and the aim of the present study will therefore be to examine the hypothesized association between anxiety/depression and IgE in a general adult female population.

Methods

A sub-sample of 374 female participants in a population-based general health study in Norway (the Hordaland Health Study) with participation rate 70% was screened for total and allergen-specific IgE. Anxiety and depression was measured employing the Hospital Anxiety and Depression Scale (HADS). This design ensured stronger statistical power than in any previous study of IgE in relation to anxiety and depression, and the population-approach ensured satisfactory variance in both IgE and anxiety/depression.

Results

No association between anxiety/depression and total IgE or anxiety/depression and allergen-specific IgE was found. Non-significant tendencies were both positive and negative. This finding was robust across continuous and categorical statistical approaches.

Conclusions

Our finding does not question the commonly reported associations between anxiety/depression and asthma, rhinitis and eczema. We do, however, question the relevance of IgE as an aetiological factor in the biological chain underlying these associations.

References:

1. Arima, M., Shimizu, Y., Sowa, J., Narita, T., Nishi, I., Iwata, N., Ozaki, N., Hashimoto, S., & Matsunaga, K. (2005). Psychosomatic analysis of atopic dermatitis using a psychological test. J Dermatol 32, 160-8.
2. Timonen, M., Jokelainen, J., Silvennoinen-Kassinen, S., Herva, A., Zitting, P., Xu, B., Peltola, O., & Rasanen, P. (2002). Association between skin test diagnosed atopy and professionally diagnosed depression: a Northern Finland 1966 Birth Cohort stu.

NR49 Monday, May 22, 9:00 AM - 10:30 AM

Homocysteine and Eating Disorders

Helge Frieling, M.D. *University of Erlangen-Nuremberg, Department of Psychiatry and Psychotherapy, Schwabachanlage 6, Erlangen, 91054, Germany*, Birgit Röschke, Martina de Zwaan, M.D., Julia Wilhelm, M.D., Stefan Bleich, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize basic neurobiological traits of anorexia and bulimia nervosa. He should know about the impact of the 1-carbon metabolism on different symptoms of eating disorders.

Summary:

Introduction:

Elevated homocysteine levels were found in various neuropsychiatric disorders (i.e. Alzheimer's disease, depression, alcohol dependence) and have been associated with depressive and neuro-cognitive symptoms. The aim of the present study was to investigate whether (i) homocysteine serum levels are elevated in women with eating disorders and (ii) if elevated homocysteine levels are linked with depressive symptoms and cognitive impairments commonly occurring in these diseases.

Methods:

Homocysteine, folate and vitamin B12 concentrations were assessed in 18 females with anorexia nervosa (AN) and 27 females with bulimia nervosa (BN) meeting ICD10 criteria. All patients were inpatients in a psychosomatic hospital. Depressive symptoms were assessed using Beck's Depression Inventory (BDI); the cut-off for clinical relevant depression was fixed at 18. A neuropsychologic battery was used to determine cognitive performance in 14 females with AN and 12 females with BN.

Results:

(i) We observed significantly (T=2.46, P=0.018) higher levels of homocysteine in anorectic patients (14.07 ± 7.3 μmol/l; mean ± SD) when compared with those suffering from bulimia (10.25± 2.82). Plasma levels of folate and vitamin B12 did not differ between groups. (ii) Significantly elevated plasma homocysteine levels were observed in patients with depressive symptoms (t-test: T=2.9, df: 42; P<0.01). Using a multivariate model, only plasma levels of homocysteine above 10.5 μmol/l predicted depressive symptoms (OR=1.38, CI 1.04-1.84, P<0.05). (iii) moderately elevated plasma homocysteine levels were associated with normal short- and long-term verbal memory while normal plasma homocysteine levels were associated with poorer memory performance (logistic forward regression Wald $\chi 2$=8.566, OR=24.75, CI 2.89-212.23.0, P<0.01).

Discussion:

Elevated homocysteine levels are only present in women with anorexia nervosa. As hypothesized, homocysteine levels were correlated with depressive symptoms. Surprisingly, under the special circumstances of eating disorders, elevated homocysteine levels improve memory signaling. These results indicate that hyperhomocysteinemia influences cognition and depressive symptoms by distinct pathways.

References:

1. Bottiglieri T, Laundy M, Crellin R, Toone BK, Carney MW, Reynolds EH: Homocysteine, folate, methylation, and monoamine metabolism in depression. J Neurol Neurosurg Psychiatry, 2000, 69:228-232.
2. Lena SM, Fiocco AJ, Leyenaar JK: The role of cognitive deficits in the development of eating disorders. Neuropsychol Rev, 2004, 14:99-113.

NR50 Monday, May 22, 9:00 AM - 10:30 AM

Affective Modulation of External Misattribution Bias in Schizophrenia

Sergi G. Costafreda, M.D. *London*, Gildas Brébion, Ph.D., Philip K. McGuire, M.D., Paul Allen, Ph.D., Cynthia H.Y. Fu, M.D.

Educational Objectives:

We present new research that we believe is relevant to the patophysiology of positive symptoms in schizophrenia. Participants to the poster session would be able to discuss with the presenter and inform themselves on the theoretical background of our work, the methods used in our experiment and the implications of our findings for the phenomenology of schizophrenia.

Summary:

Introduction: It has been observed that schizophrenic patients have a bias towards attributing self-produced words to an external source. This could underlie the production of symptoms such as auditory hallucinations. We sought to investigate whether this external misattribution bias was modulated by emotional valence. We hypothesised that emotional words would be associated with more external misattribution Extended Release rors and that this association would be stronger in symptomatic patients. Method: 30 schizophrenic patients were classified as hallucinator or non-hallucinator, delusional or non-delusional, and psychotic or remitted according to the relevant scores in the Scale for the Assessment of Positive Symptoms (SAPS). The subject and the experimenter alternately read a list of 48 words, designed to contain half neutral and half affective words. The experimenter then randomly presented the same words while the subject decided whether he or the experimenter had generated them. The study was analysed as a repeated measures ANOVA with two within subject variables (source of the utterance and emotional valence) and a between subject variable (group). Results: Consistent with earlier reports, external misattribution was more common than other types of attributional Extended Release rors ($p<0.05$). Emotionally loaded words exacerbated this bias compared to neutral words ($p<0.05$). This bias was greater for delusional versus non delusional, hallucinators versus non-hallucinators and psychotic versus remitted patients ($p<0.05$). Psychotic patients were more prone to this potentiation of the bias by emotional words than remitted patients, although the difference was marginally non-significant ($p=0.07$).

Discussion: We have replicated previous findings of an external misattribution bias in schizophrenic patients, especially when suffering from active symptoms. To our knowledge, this is the first report of an emotional modulation of this bias. This finding may have implications in our understanding of the physiopathology of symptom production in schizophrenia.

References:

1. Brebion G, Amador X, David A, Malaspina D, Sharif Z, Gorman JM: Abstract Positive symptomatology and source-monitoring failure in schizophrenia--an analysis of symptom-specific effects. Psychiatry Res. 2000 Aug 21;95(2):119-31.
2. Allen PP, Johns LC, Fu CH, Broome MR, Vythelingum GN, McGuire PK: Misattribution of external speech in patients with hallucinations and delusions. Schizophr Res 2004;69:277-87.

NR51 Monday, May 22, 9:00 AM - 10:30 AM

Pragmatic Considerations in the Comorbid Presentations of Anxiety Disorder and Substance Use Disorder in Patients With Rapid Cycling Bipolar Disorder

Keming Gao, M.D. *University Hospitals of Cleveland, Psychiatry, 11400 Euclid Ave., Suite 200, Cleveland, OH, 44106*, Steven J. Ganocy, Ph.D., Sarah Bilali, M.A., Carla Conroy, B.A., Joseph R. Calabrese, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the different presentations of anxiety disorder and substance use disorder in patients with rapid cycling bipolar I or II disorder.

Summary:

Objective: To study comorbid anxiety disorder (AD) and substance use disorder (SUD) in rapid cycling bipolar disorder (RCBD). **Method:** Data of patients in our research studies were analyzed for the comorbid presentations of AD and SUD. The rates of GAD, panic disorder (PD), and OCD were compared between BPI and BPII in the "None" group - no history of SUD, the "Lifetime, but not recent" group - history of SUD, but not using within last 6 months, and the "Recent" group - history of SUD with using within last 6 months. **Results:** In the "None" group (BPI n=84, BPII n=107), patients with BPI and BPII had comparable rates of GAD (31 % versus 29%), PD (26% versus 26%), and OCD (13% versus 8%). In the "Lifetime, but not recent" group(BPI n=102, BPII n=93), patients with BPI had significantly higher rates of GAD (44% versus 19%) and PD (34% versus 15%), but not OCD (6% versus 5%) than their BPII counterparts. Similarly, in the "Recent" group (BPI n=134, BPII n = 46), patients with BPI had significantly higher rates of GAD (51% versus 22%) and PD (38% versus 13%), but not OCD (6% versus 4%). The odds ratios of patients with BPI to BPII for an AD were 1.12 in the "None" group, 2.7 in the "Lifetime, but not recent", and 3.6 in the "Recent." **Conclusion:** Different presentations of AD and SUD existed between patients with BPI and BPII. A positive association between AD and SUD occurred only in patients with BPI.

References:

1. McElroy SL, Altshuler LL, Suppes T et al. Axis I psychiatric comorbidity and its relationship to historical illness variables

in 288 patients with bipolar disorder. Am J Psychiatry 2001; 158: 420-426.

2. Brown ES, Suppes T, Adinoff B et al. Drug abuse and bipolar disorder: comorbidity or misdiagnosis? J Affect Disord 2001; 65:105-115.

NR52 Monday, May 22, 9:00 AM - 10:30 AM

The Influence of Maternal and Child Anxiety on Mother-Child Interactions

Natalie S. Gar *Macquarie University, Linguistics and Psychology, 6/100 Birriga Rd., Bellevue Hill, Sydney, New South Wales, 2023, Australia*, Jennifer L. Hudson, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to demonstrate an understanding of the parental characteristics that have been implicated in past research with the anxiety disorders, and to understand how the nature of a certain research task may influence the parent-child interaction.

Summary:

The purpose of this study was to examine whether having an anxious child influences the degree of maternal involvement and negativity in a population of nonanxious mothers. In addition, this study investigated whether maternal anxiety influences the degree of maternal involvement and negativity in a population of anxious children. 86 mother-child dyads were observed while the child (aged 7-17) completed a speech task. The sample consisted of three diagnostic groups: (1) nonanxious children with nonanxious mothers, (2) anxious children with nonanxious mothers, and (3) anxious children with anxious mothers. Anxious children were recruited from the Macquarie University Anxiety Research Unit, Sydney, Australia. Nonanxious children were recruited from the surrounding community. In contrast to previous findings, results showed no significant differences in involvement or negativity between the nonanxious mothers with nonanxious children and nonanxious mothers with anxious children, and no significant differences between nonanxious mothers with anxious children and anxious mothers with anxious children. This study failed to provide support for the association between maternal overinvolvement and negativity and the anxiety disorders. However, this data does support previous research which suggested that mothers may not be uniformly overinvolved and critical but may only respond that way in certain situations. The observational examination of the parent-child interaction and of the impact of child and parent anxiety in this uniquely designed speech task has important implications for the treatment of anxiety disorders. This study was funded by the Australian Research Council.

References:

1. Hudson JL, Rapee, RM: Parent-child interactions and anxiety disorders: An observational study. Behaviour Research and Therapy 2001; 39: 1411-1427.

2. Hudson JL, Rapee, RM: Parent-child interactions in clinically anxious children and their siblings. Journal of Clinical Child and Adolescent Psychology 2002; 31:548-555.

NR53 Monday, May 22, 9:00 AM - 10:30 AM

Quetiapine as Monotherapy for Social Anxiety Disorder

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Educational Objectives:

At the end of this poster presentation, the viewer should be able to appreciate the rationale for using quetiapine as monotherapy for social anxiety disorder. The viewer should be able to understand the trial design as well as the results obtained.

Summary:

Objective: Social anxiety disorder (SAD) is characterized by fear and avoidance of social or performance situations. SAD is the most common anxiety disorder in the US. First line pharmacotherapy is generally a selective serotonin reuptake inhibitor (SSRI), although treatment effects are often small. Quetiapine is a novel atypical antipsychotic drug with greater occupancy at serotonergic vs. dopaminergic receptors. Several reports have suggested an effect for quetiapine in anxiety disorders. Given these considerations, we conducted a double-blind, placebo-controlled pilot trial of quetiapine in SAD.

Method: Subjects were randomized in a 2:1 ratio to treatment with either quetiapine (up to 400 mg/day) or placebo for 8 weeks. Of 14 subjects who completed the trial to date, 13 provided evaluable data. Key outcome measures included the Brief Social Phobia Scale (BSPS) and the Clinical Global Impression of Improvement (scale (CGI-I).

Results: Utilizing an intent-to-treat, last observation carried forward analysis, mean BSPS scores changed from 44.5 at baseline to 31.4 at week 8 in the quetiapine group vs. 47.5 to 36.8, respectively, in the placebo group. Mean BSPS scores for the treatment groups were comparable at baseline and the effect size between treatments at endpoint was moderate at 0.50. Rates of response (defined as a CGI-I of 1 or 2) were 44% for quetiapine (4/9) and 0% for placebo (0/4). The number needed to treat to demonstrate much or very much improvement in SAD symptoms was 3 (95% CI 1.3, 8.3). There were no major adverse events.

Conclusions: Data from this small 8-week controlled pilot trial suggest that quetiapine may have a role in treating SAD. Larger controlled trials of quetiapine in SAD are warranted.
Funding support was provided by AstraZeneca.

References:

1. Hildalgo, RB, Barnett, SD, Davidson JR: Social anxiety disorder in review: two decades of progress. Int J Neuropsychopharmacol 2001; 16:279-298

2. Atmaca M, Tezcan E, Gecici O: Quetiapine augmentation in patients with treatment resistant obsessive-compulsive disorder: a single-blind, placebo-controlled study. Int Clin Psychopharmacol 2002; 17:115-119

NR54 Monday, May 22, 9:00 AM - 10:30 AM

ADD Comorbidity in Adults

John Andrew A. Gergen, M.D. *retired Univ Il Col Med at Urbana-Champaign, Psychiatry, 250 Pantops Mtn Rd #5107, Charlottesville, VA, 22911*

Educational Objectives:

At the conclusion of this presentation, the participant should recognize some of the behavioral traits present in adults with an attention deficit disorder who have a comorbid psychiatric disorder, to recognize the likelyhood that this comorbidity may be particularly reflected in bipolar II and bipolar spectrum or in substance abuse disorders and that the presence of this comorbidity may require consideration in developing a successfull treatment plan. It should also further the recognition that psychiatric comordities with adult ADD may be quite common consistent with estimates that 8% of the population has ADD elements in their personality structure which persist into adulthood while other estimates suggest that up to 50% of persons with ADD develope a psychiatric disorder during their lifetime.

Summary:

Clinical observations suggest that the genetic factor(s) driving Attention Deficit Disorders (ADD) is a trait with both positive and negative consequences. Trait characteristics identified in other settings include persisting difficulties in sustained attention with easy distractability accompanied by other abilities to hyperfocus on areas of interest, an all-or-none quality to memory and emotional states, an unexpected recall of trivia, problems working under supervision but potential success as a leader or a loner, an unusual talent or intuitive ability in one or more areas and a positive family history consistent with trait presence. This report summarizes findings for 75 adult psychiatric outpatients who had a psychiatric disorder with suggestions of comorbidity with ADD based on a history of trait presence but then participating in a confirmatory evaluation by a written questionnaire (1). Of these individuals, 64% were confirmed, 32% were highly likely and 4% unconfirmed for ADD. The final comorbid diagnostic conclusions in descending order were a bipolar II or bipolar unspecified disorder (78%), a history of substance abuse (43%), a panic or anxiety disorder (32%) and to lesser extents, obsessive compulsive issues, chronic pain from various sources, other forms of a mood disorder and PTSDs. Other frequent characteristics of this group included positive responses only with higher doses of SSRIs but generally better outcomes with mood stabilizers, buproprion and other adrenergic promotors.

(1) AmenDG: General Adult ADD Symptom Checklist. In Attention Deficit Disorder In Intimate Relationships. Mind Works Press,1997, pp 33-39.

References:

1. Amen DG: general Adult ADD Symptom Checklist. In Attention Deficit Disorder In Intimate Relationships Fairfield, CA., Mind Works Press, 1977, pp33-39.
2. Hallowell EM, R atey JJ: Delivered from Distraction. New York, Ballantine Books, 2005.

NR55 Monday, May 22, 9:00 AM - 10:30 AM

Reproductive Losses and Perinatal Depression

Stephanie A.M. Giannandrea *University of Rochester School of Medicine, Psychiatry, Box Psych 4-9200, 300 Crittenden Blvd., Rochester, NY, 14642*, Linda H. Chaudron, M.D., Holly Wadkins, M.A., Elizabeth Anson, B.A., Kimberly Sidora-Arcoleo, M.P.H., Harriet J. Kitzman, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the particpant should be able to 1) recognize risk factors for perinatal depression in poor, predominantly minority women who have experienced pregnancy loss, defined as miscarriage, fetal death, still birth, and/or induced abortion, compared with women who have never experienced reproductive loss and 2) recognize risk factors for perinatal depression in women who have undergone induced abortion and involuntary pregnancy loss.

Summary:

Introduction: Spontaneous and induced abortion, childbirth, and perinatal depression are common events in the lives of low-income, minority women, but there is virtually no literature on possible relationships between these factors.

Objectives: 1) To compare risk factors for perinatal depression in poor, predominantly minority women who have experienced pregnancy loss, defined as miscarriage, stillbirth, and/or induced abortion, with women who have never experienced reproductive loss. 2) To compare risk factors for perinatal depression between women who have undergone induced abortion and involuntary pregnancy loss.

Methods: The original study was designed to validate screening tools for postpartum depression in low-income women across the first postpartum year. Women were recruited at pediatric well child-care visits from an urban pediatric clinic in an academic center. Cross-sectional data were collected from 194 women, including demographic information, questionnaires, depression screening tools, and a clinical interview. The current study is a preliminary secondary analysis of original data from 153 women to explore the relationship between pregnancy loss and subsequent perinatal depression. Data were analyzed by chi square, t-test, and linear regression using SPSS 13 for Windows. **Results**: Women who had experienced pregnancy loss did not differ significantly from women who had not in any demographic factors except older age. Women with a history of pregnancy loss were more likely to be depressed during the first postpartum year after a subsequent live birth (p=.019). Induced abortion, miscarriage, stillbirth, or multiple types of losses did not individually increase the risk of depression. **Conclusions**: Because women with a history of pregnancy loss are at increased risk for postpartum depression, they should be monitored closely for depression around the birth of a subsequent child. Follow-up visits could be scheduled during times of increased stress. In addition, earlier and more aggressive treatment should be considered in women with these risk factors.

References:

1. Broen AN, Moum T, Bodtker AS, Ekeberg O: Psychological impact on women of miscarriage versus induced abortion: a 2-year follow-up study. Psychosomatic Medicine 2004; 66:265-71.
2. Janssen HJ, Cuisinier MC, Hoogduin KA, de Graauw KP: Controlled prospective study on the mental health of women following pregnancy loss. Am J Psychiatry 1996; 153: 226-30.

NR56 Monday, May 22, 9:00 AM - 10:30 AM

Impact of Written Exposure on Worry

Natalie Goldman *Concordia University, 6931 Sherbrooke St. W., #405, Montreal, PQ, H4B 1P8, Canada*, Michel J. Dugas, Ph.D.

Educational Objectives:

At the conclusion of this poster presentation, the participant should be aware of and understand the use of writing as a method of exposure for worry. The educational objective of this new research is to recognize new methods of exposure that can be applied to the treatment of generalized anxiety disorder.

Summary:

Although written disclosure procedures lead to improvements in physical and emotional health, the relationship between writing and worry has yet to be systematically investigated. Given that cognitive avoidance is thought to play an important role in current models of GAD, writing about feared outcomes may be beneficial for high worriers because it serves as a structuring context for functional exposure, and thus may facilitate the emotional processing of fear. The goal of this study is to assess the outcome of a written exposure procedure in high worriers. We hypothesized that individuals in the written exposure condition would show greater decreases in self-reported worry than those in the control writing condition. Thirty non-clinical high worriers were randomly assigned to either a written exposure condition or a control writing condition. Participants in the written exposure condition (n=15) were instructed to write scenarios describing their worst fear coming true and to describe their emotional, cognitive and behavioral reactions to the situation in the first person, present tense. Participants in the control condition (n=15) wrote about a neutral, hypothetical and future situation in an unemotional and objective way. All participants wrote for 30 minutes each day over 5 consecutive

days. Self-report measures were used to assess worry, anxiety, depression and intolerance of uncertainty (IU) at 4 points during the study: pretest, posttest, and 1- and 2-week follow-ups. Preliminary statistical analyses reveal a significant decrease in worry and depression from pretest to 2-week follow-up in the written exposure group but not in the control group. Additionally, results show a significant decrease in IU from pretest to posttest in the written exposure group but not in the control group. As hypothesized, written exposure leads to significant reductions in worry. Implications of these findings in the treatment of GAD are discussed.

References:

1. Dugas MJ et al.: Group cognitive-behavioral therapy for generalized anxiety disorder: Treatment outcome and long-term follow-up. J Consult Clin Psychol 2003; 71: 821-825.
2. Foa EB & Kozak MJ: Emotional processing of fear: Exposure to corrective information. Psychol Bull 1986; 99: 20-35.

NR57 Monday, May 22, 9:00 AM - 10:30 AM

A Gender-Focused Epidemiologic Perspective on Health Service Utilization in Comorbid Bipolar I Disorder and Alcohol Use Disorder

Benjamin I. Goldstein, M.D. *University of Toronto, Psychiatry, 2075 Bayview Avenue, Room 646, Toronto, ON, M4N 3M5, Canada*, Anthony J. Levitt, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to:

1. Recognize the under-utilization of health services by individuals with comorbid BD and AUD.
2. Identify gender-specific patterns of service utilization in this population.
3. Appreciate the potential role of gender biases in perpetuating these patterns.

Summary:

Objectives: This study compares health service utilization by individuals with comorbid lifetime bipolar I disorder (BD) and lifetime alcohol use disorders (AUD) to that of individuals with either diagnosis alone, using nationally representative data.

Methods: The National Epidemiologic Survey on Alcohol and Related Conditions was used to identify respondents with BD-only (N=636), AUD-only (N=11,068), and comorbid BD-AUD (N=775). These three groups were compared with respect to self-reported health service utilization.

Results: For both men and women, respondents in the BD-AUD group were significantly more likely than AUD-only respondents to report any alcohol-related service utilization. However, there was a significantly greater prevalence of alcohol dependence in the BD-AUD group than in the AUD-only group. Comorbid BD-AUD respondents were significantly more likely to report BD-related hospital admissions as compared with BD-only respondents amongst males only. Within the BD-AUD group, males reported significantly greater utilization of AUD treatment only, and females reported significantly greater utilization of BD treatment only and significantly greater likelihood of utilizing mental health services overall. There was no gender difference in the proportion of respondents who utilized both AUD and BD services.

Conclusions: As expected, individuals with comorbid BD and AUD utilize significantly more mental health services than individuals with either disorder alone. The primary original finding is that among those with comorbid BD-AUD, BD is more likely to go untreated among males and AUD is more likely to go untreated among females.

References:

1. Verduin ML, Carter RE, Brady KT et al: Health service use among persons with comorbid bipolar and substance use disorders. Psychiatr Serv 2005; 56:475-480.
2. Bauer MS, Shea N, McBride L: Predictors of service utilization in veterans with bipolar disorder: a prospective study. J Affect Disord 1997; 44:159-168.

NR58 Monday, May 22, 9:00 AM - 10:30 AM

Pregnancy Exposures: Mothers Recall vs Prospective Documentation

Paula Green, B.A. *Emory University, Psychiatry, 1365 Cifton Rd, Ste 6100, Atlanta, GA, 30322*, Zachary N. Stowe, M.D., Patricia Brennan, Ph.D., Natalie Morris, D. Jeffrey Newport, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant will be familiar with the limitations of maternal retrospective recall in providing accurate information on illness and medication exposures. This will help place previous investigations/reports in proper perspective with respect to driving clinical care.

Summary:

Previous investigations have demonstrated that retrospective recall bias leans toward positive experiences (Walker, WR et al. 2003). Studies of the impact of antidepressant exposure and maternal depression have often relied on single point assessments or retrospective recall of medication and symptom exposures. The accuracy of such recall is pivotal in delineating the impact of both medication use and depression on obstetrical outcome. A total number of 164 pregnant women enrolled in a prospective study (total of 807 prenatal visits) of antidepressant exposure and maternal depression at the Emory Women's Mental Health Program. At six months postpartum, the women were interviewed regarding all exposures during pregnancy including mental illness and medications, and queried on a month-by-month basis. Maternal depressive symptoms during pregnancy were compared using prospectively obtained measures (BDI, HRSD, SCID mood module) and postpartum interview results. In our initial analysis, we utilized a BDI score of ≥14 to represent significant depressive symptoms (as confirmed in our factor analysis in a separate investigation Bruce et al). Women with BDI scores throughout pregnancy of <14 retrospectively reported being depressed 10.1% of the time. In contrast, women with BDI scores >13, retrospectively denied being depressed 57.8% of the time. The positive predictive value for a retrospective yes for depression during pregnancy was 68.2% and the negative predictive value for a retrospective no was 75.0%. Preliminary analysis suggests that medication exposure recall may be equally limited. Additional analysis will include diagnostic criteria, and medication exposures. These results underscore the value of prospective investigations to document maternal depression during pregnancy, particularly in determining the factors associated with outcome. Supported by NIH P50 MH68036, P50 MH58922

References:

1. Walker WR, Skowronski JJ, Thompson CP. Life is Pleasant--and Memory Helps to Keep it That Way. General Psychology 2003; 7(2): 203-210.
2. Cramer JA, Rosenheck, R: Enhancing Medication Compliance for People with Serious Mental Illness. J Nervous Mental Disease 1999;187(1):53-55.

NR59 Monday, May 22, 9:00 AM - 10:30 AM

Relationship of Disinhibition and Aggression to Blunted Prolactin Response to Meta-Chlorophenylpiperazine in Patients With Cocaine Dependence

Kevin P. Hill, M.D. *Yale University School of Medicine, IE-61 SHM, P.O. Box 208088, New Haven, CT, 06520-8088*, Ashwin A. Patkar, M.D., Paolo Mannelli, M.D., Rano Thomas Matthew, M.D., Kathleen Peindl, Ph.D., Haresh Tarwani, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that cocaine-dependent patients show disturbances in postsynaptic 5-HT function during early abstinence. These disturbances are more pronounced in the subgroup of cocaine patients with high disinhibition and aggression.

Summary:

Rationale: Considerable evidence indicates that serotonergic (5-HT) mechanisms may mediate central effects of cocaine, and disinhibition and aggression. **Objective:** We investigated whether prolactin (PRL) response to meta-chlorophenylpiperazine (m-CPP), a mixed 5-HT agonist/antagonist, differed between abstinent cocaine-dependent patients and controls, and whether m-CPP challenge responses were related to measures of disinhibition and aggression. **Methods:** 35 cocaine-dependent African-American subjects who were abstinent for at least 2 weeks and 33 African-American controls underwent assessments of disinhibition and aggression and a challenge with 0.5 mg/kg of oral m-CPP. **Results:** The PRL response to m-CPP was compared between cocaine patients and controls and between subgroups categorized high or low based on disinhibition and aggression measures. Hierarchical regressions were used to determine whether behavioral measures predicted ΔPRL (peak PRL -baseline PRL). The PRL response to m-CPP was significantly diminished in cocaine patients compared to controls. The blunting was more robust in cocaine patients with high disinhibition and aggression. Among cocaine patients, the high disinhibition subgroup showed greater blunting than the low disinhibition subgroup and there was a trend for the high aggression subgroup to be more blunted than the low aggression subgroup. The subgroups of controls did not differ from each other. A combination of disinhibition and aggression measures significantly predicted ΔPRL in cocaine patients. **Conclusion:** The results indicate that cocaine dependent patients show disturbances in postsynaptic 5-HT function during early abstinence. It appears that the 5-HT disturbances are more pronounced in the subgroup of cocaine patients with high disinhibition and aggression.

References:

1. Buydens-Branchey L, Branchey M, Fergeson P, Hudson J, McKernin C: The meta-chlorophenylpiperazine challenge test in cocaine addicts: hormonal and psychological responses. Biol Psychiatry 1997; 41:1071-1086.
2. Coccaro EF, Kavoussi RJ, Hauger RL: Physiological responses to d-fenfluramine and ipsapirone challenge correlate with indices of aggression in males with personality disorders. Int Clin Psychopharmacol 1995;10: 177-179.

NR60 Monday, May 22, 9:00 AM - 10:30 AM

Prolactin Serum Levels as a Useful Method to Asses the Risk of Alcohol Withdrawal Seizures

Thomas Hillemacher, M.D. *University of Erlangen, Psychiatry and Psychotherapy, Schwabachanlage 6, Erlangen, 91054, Germany*, Helge Frieling, M.D., Kristina Bayerlein, M.D., Julia Wilhelm, M.D., Johannes Kornhuber, M.D., Stefan Bleich, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to understand the present findings regarding the association of elevated prolactin serum levels and the risk of alcohol withdrawal seizures.

Summary:

Introduction: Serum prolactin levels have been discussed as a useful method for differential diagnosis in epilepsia. The present study was undertaken to investigate the association between previous alcohol withdrawal seizures and prolactin serum levels.

Methods: 118 male patients admitted for detoxification treatment and suffering from alcohol-dependency were included in the study. Previous withdrawal seizures were recorded and used as reference for the risk of alcohol withdrawal seizures. None of the patients suffered from an actual seizure because all patients were treated with carbamazepine. Prolactin serum levels were measured using an enzymatic immunoassay.

Results: Significantly higher prolactin levels (17.8ng/ml, SD 12.1) were found in patients with a history of alcohol withdrawal seizures than in patients without previous seizures (13.0ng/ml, SD 8.1, $p<.05$). Also, multivariate logistic regression revealed significant predictive qualities for prolactin serum levels (B = .05, Wald = 5.30, p = .021, OR = 1.06, 95%CI = 1.01-1.11).

Conclusion: The present study shows for the first time an association between elevated prolactin serum levels and a history of withdrawal seizures. Hence, the results suggest that prolactin elevation at admission may be a clinical marker for an increased risk of withdrawal seizures which should be subject to further research.

References:

1. Anzola GP: Predictivity of plasma prolactin levels in differentiating epilepsy from pseudoseizures: a prospective study. Epilepsia 1993; 34:1044-1048.
2. Bayerlein K, Hillemacher T, Reulbach U, Mugele B, Sperling W, Kornhuber J, Bleich S: Alcoholism-associated hyperhomocysteinemia and previous withdrawal seizures.Biol Psychiatry 2005; 57: 1590-1593.

NR61 Monday, May 22, 9:00 AM - 10:30 AM

Mood Stabilizers and Depression in the Postpartum Period

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Educational Objectives:

At the conclusion of this session, the participant should be able to be familiar with prospective data of depressive symptoms during the postpartum period, placental passage of mood stabilizers, and implications for treatment planning for at risk populations.

Summary:

Both patients with Bipolar Disorder (BPD) and Epilepsy are likely to be treated with mood stabilizers in pregnancy and the postpartum period. Managing BPD during the postpartum period presents a complicated treatment evaluation. Establishing effective treatment planning for both groups over the perinatal period is an unmet clinical need.

In the current study, 116 pregnant women (61 with BPD, 51 with Epilepsy) were followed prospectively through pregnancy (<20 weeks) and the postpartum period. Subjects completed the Hamilton Rating Scale for Depression (HRSD) at follow up visits. A threshold of 15 was employed to identify significant depressive

symptoms. The HRSD mean and proportion crossing the threshold during late pregnancy and the early postpartum period were compared between diagnostic groups and individual medications. Significant differences were found in HRSD scores for bipolar and epileptic subjects for their last visit during pregnancy (lamotrigine: 11.4±3.7 versus 8.9±4.6; other mood stabilizers 13.5±6.9 versus 8.1±3.5, respectively). These differences continued during the postpartum period (lamotrigine: 12.1±4.7 versus 8.7±5.3; other mood stabilizers 13.3±8.3 versus 8.9±4.2, respectively). The number of women with BPD and a HRSD>14 was similar between medication groups - 6 of 15 (40%) with lamotrigine, 9 of 23 (39%) with lithium, and 11 of 23 (48%) with other mood stabilizers. In contrast, initial analysis utilizing depression scales (BDI, HRSD) as a continuous variable in women with epilepsy treated with lamotrigine had lower depressive symptoms during the postpartum compared to other antiepileptic drugs. Analysis of obstetrical outcome and placental passage will be discussed. The contribution of individual subject variability in treatment will be discussed with an emphasis on delineating optimal treatment strategies for postpartum women taking mood stabilizers.

These data underscore the need to critically evaluate treatment strategies in women treated with mood stabilizers to reduce postpartum depressive symptoms.

Supported by P50-MH-68036 and R01-MH-71531

References:

1. Pennell PB: Antiepileptic Drug Pharmacokinetics During Pregnancy and Lactation. Neurology 2003; 61(2): 35-42.
2. Stowe ZN, Hostetter A, Newport DJ: The onset of postpartum depression: Implications for clinical screening in obstetrical and primary care. Am J Obstet Gynecol 2005; 192(2): 522-6.

NR62 Monday, May 22, 9:00 AM - 10:30 AM

Antipsychotic Prescribing Trends: Pre- and Post-Publication of Effectiveness of Antipsychotic Drugs in Patients With Phase I Chronic Schizophrenia

Rachel A. Houchins, M.D. *Palmetto Health and Universtiy of South Carolina, Neuropsychiatry, 108 Brandon Hall Road, Columbia, SC, 29229*, John J. Buckland, D.O., Joseph D. Markowitz, M.D., Christine Latham, R.Ph., Meera Narasimhan, M.D., Richard K. Harding, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to: **(1)** Recognize the impact of the CATIE trial on the prescribing trends of antipsychotic medications. **(2)** Note differences in both the trends among typicals versus atypicals as well as individual agents in these groups. **(3)** Recognize demographics of the population as well as diagnoses. **(4)** Recognize the complexity of the schizophrenic population that at times necessitates the use of more than one antipsychotic. **(5)** Observe the rate of polypharmacy in this population. **(6)** Address the shortcomings of the CATIE trial including the applicability to chronic schizophrenia and the implications for future formulary changes and patient care.

Summary:

Objective: To determine if prescribing trends of antipsychotics have changed since publication of CATIE phase I.

Background: The CATIE study addressed the relative effectiveness of atypical antipsychotics compared to the typical antipsychotic, perphenazine. Conclusions suggested that the efficacy of perphenazine was similar to the atypicals.

Methodology: This study will identify differences in antipsychotic prescribing among adult inpatients diagnosed with schizophrenia, schizoaffective, or psychosis NOS before and after publication of CATIE. Focuses include comparing typical versus atypical rates and delineating between specific agents in both classes, including perphenazine. Data will be analyzed by logistical regression to show statistically significant changes in the 6 months pre-publication versus post-publication.

Results: Preliminary data one month pre-publication and one month post-publication were examined. There were 40 patients in the pre and 24 in the post-publication groups. Demographic data revealed average age of 40.45 and 40.67 pre and post-publication, race 65% African American pre and 62.5% post-publication, and sex 50% female pre and 20.8% post-publication.

Data regarding the medications revealed: 1. The pre-publication group tended to be treated with fewer typicals as first-line: 7.5 % versus 12.5% post-publication. 2. A difference among the atypicals with aripiprazole increasing as initial treatment from 12.5% of the pre to 25% of the post-publication. 3. Risperidone was the most common first-line agent in both groups, 32.5% and 29.2% respectively. 4. 62% of the study participants were prescribed more than one antipsychotic during hospitalization. 5. A trend in the post-publication group towards increasing use of typical agents as a second-line with only 16% of second-line agents being typicals in the pre-publication group and 40% being typicals in the post-publication group.

Conclusion: There was a trend towards increasing use of typical agents as both first and second-line treatment in the psychotic disorders, which warrants further investigation.

References:

1. Lieberman, Jeffrey A., Stroup, Scott, McEvoy, Joseph et al. Effectiveness of Antipsychotic Drugs In Patients with Chronic Schizophrenia. The New England Journal of Medicine. 2005, Sept353:1209-1223.
2. Leucht S, Barnes, TRE, Kissling, W, Engel RR, et al. Relapse prevention in schizophrenia with new-generation antipsychotics: a systematic review and exploratory metanalysis of randomized controlled trials. American Journal of Psychiatry 2003, 1.

NR63 Monday, May 22, 9:00 AM - 10:30 AM

Pseudo-Odor Induced Pseudo-Seizures

Haridia Hristea, M.D. *Rush University Medical Center, Psychiatry & Neurology, 2801 South King Drive, # 614, Chicago, IL, 60616*, Alan R. Hirsch, M.D.

Educational Objectives:

Demonstrate somatic and psychological manifestation of pseudo-odor

Summary:

Objective: Demonstrate somatic and psychological manifestation of pseudo-odor.

Method: Case study

Results: The belief of the presence of an odor in the absence of a true odor has been demonstrated to cause a variety of physical complaints.

A case of pseudo-seizures induced by pseudo-odor is reported.

A 38yo woman presented with a six month history of odor induced spells. These occurred in response to a wide range of common odors. Thirty minutes after exposure she experiences right nostril tingling, ocular pain, and hemicephalgia. This intensifies and she becomes presyncopal, vertiginous and atonic, without tongue biting and urinary incontinence. She then displays clonic movements of one arm and one leg, which when externally stopped, transfers to the contralateral extremities. Episodes last for half an hour and they are followed by apnea or hyperventilation, unresponsiveness and postictal paralysis. Afterwards, she is able to write but not speak. When speech returns, there appears a thick Russian accent, which persists for one day. These episodes have precipitated frequent hospitalizations, all concluding no evi-

dence of organiz pathology. This condition has caused extreme avoidance of environments laden with odor, to the point of agoraphobia.

While under EEG monitoring, patient was exposed to an odorless bottle and in response, she developed the above-described behavior, in the absence of changes on EEG or neurological signs of seizures (positive Babinski sign, changes in reflexes, nystagmus, absent opticokinetic-induced nystagmus)

Conclusion: This demonstrates the nocibo effects of a pseudo-odor and the potential risk of precipitating similar episodes in response to olfactory testing in such individuals.

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NR64 Monday, May 22, 9:00 AM - 10:30 AM

Alterations of Function and Expression of Cyclic AMP Response Element-Binding Protein in Peripheral T Lymphocyte of Patients With Depression During a 24-Week Treatment With Fluoxetine

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that the therapeutic effect of chronic antidepressant administration is correlated with cell adaptation mechanism through CREB expression and CRE-DNA binding.

Summary:

Objects : The therapeutic procedure of several antidepressants develop a time lag of 4 to 6 weeks. Such a time lag is known as contain the several signal transduction pathways in post-synapse after targeting antidepressant to 5HT transporter, primary target of SSRI. Our study aims at elucidating the alterations and adaptable changes of signaling pathway in post-synapse after chronic antidepressant treatment.

Design: We studied the changes between drug-responsive and the expression and function of transcription factor, CREB in peripheral lymphocytes of depressed patients at 0, 6 and 24weeks, during SSRI antidepressant treatment

Methods : CREB-expression and phosphorylation was quantified via immunoblot, and binding activity between transcription factor and DNA via electrophoretic mobility shift assay(EMSA) in nuclear extracts from 35 depressed patients at 0, 6 and 24th week during fluoxetine treatment(10mg/day). Drug response was quantified as HAM-D score. The correlations between alterations of CREB characteristics and drug response during drug treatment were analyzed by Pearson or Spearman's rho correlation using SPSS11.0.

Results : During 6 weeks of antidepressant treatment, the change of HAM-D score correlated with the CREB expression and phosphorylation(r=0.618, p=0.018; r=0.645, p=0.013, respectively). The change of CREB and CRE-DNA binding during 0 ~ 6 weeks correlated negatively with during 6 ~ 24 weeks(r=-0.456, p=0.050;r=-0.670,p=0.002 by Spearmann's rho). During 0 ~ 6 and 6 ~ 24 weeks, respectively, CREB expression, pCREB expression, and CRE-DNA binding were positively correlated each other.

Conclusions : We suggest CREB expression and CRE-DNA binding might undergo cell adaptation during 24 weeks of antidepressant treatment. Furthermore, explored this study for the longer periods, it would be possible to elucidate the cell adaptation mechanism

via drug treatment.

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NR65 Monday, May 22, 9:00 AM - 10:30 AM

Appetite Change and Alzheimer's Disease

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Educational Objectives:

(1) To review appetite as a component of the behavioural and psychological symptoms of dementia in Alzheimer's disease.

(2) To investigate brain regions of interest as they pertain to appetite change in Alzheimer's disease.

Summary:

Objectives: In addition to the cognitive deficits in Alzheimer's Disease (AD) non-cognitive behavioral and psychological symptoms of dementia (BPSD) are also implicated in morbidity and functional decline. One of these BPSD domains is appetite. Studies have shown that some patients with AD have appetite disturbance but the mechanism is unclear. This study is aimed to investigate the possible association of regional cerebral perfusion and appetite change in AD.

Methods: 57 patients (27 male, 30 female; mean ± SD age, 79.4 ± 5.4) with probable AD or mixed Dementia (NINCDS-ADRDA criteria; MMSE 22.9 ± 4.1) were characterized as with (n= 12) or without (n=45) appetite loss based on the Cornell Scale for Depression in Dementia Appetite Subscale (score ranges 0-2). 99mTc-ECD single photon emission computer tomography (SPECT) scans were coregistered to a standardized template in Talairach space generating mean ratios of uptake referenced to the cerebellum and providing semiquantitative regional perfusion ratios for each patient. Based on previous neuroimaging studies, the bilateral regions of interest (ROI) chosen *a priori* were the anterior cingulate cortex (ACC), middle mesial temporal cortex (MTC-m), inferior mesial temporal cortex (MTC-i) and insula (INS).

Results: A backward stepwise regression analysis of these ROI's showed hypoperfusion in the L-ACC (p=0.10), relative hyperperfusion in the R-ACC (p=0.05), and hyperperfusion in the L-MTC-m (p=0.04) predicted loss of appetite (F=3.2, p=0.03). This model had an R of 0.39 accounting for 15.3% of the variance.

Conclusions: The ACC and MTC-m may have a role in regulating appetite in this sample of patients with AD. These preliminary data are part of an ongoing study and sample size will be increased.

References:

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PET study. Prog Neuropsychopharmacol Biol Psychiatry 2002; 16: 1285-1289.

NR66 Monday, May 22, 9:00 AM - 10:30 AM

Maternal Psychological State and Family Environments of Children With Juvenile Diabetes and Depressive Mood Disorder

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand that the psychological state of mothers with diabetic children may influence their children's adaption to diabetes.

Summary:

Objectives : The aim of this study was to examine the characteristics of demographic variables, maternal psychologic state and family environments of juvenile diabetes children with depressive mood.

Methods: Among IDDM patients who participated in diabetes camp which was held in Taegu in 2004, the author sent questainnaires which included CDI/BDI for children, MMPI and SCL-90 for patients' mothers, and FES which mothers were asked to respond to the 40 patients' house after gaining parents and patients' permission by telephoning. Among 40 patients, 23 patients completed these questainnaires. Among 23 patients, 10 boys and 13 girls attended this study.

Results: The results are as follows : There were significant differences in maternal MMPI and SCL-90 between depressive IDDM patients group and non-depressive patients group. Among the maternal MMPI, the t-scores of Hypochondriasis and hysteria of depressive IDDM group were higher than those of non- depressive IDDM group. And among the dimension of SCL-90, t-score of depression, anxiety, phobic anxiety and psychoticism of depressive IDDM group were higher than those of non-depressive IDDM group($p < 0.05$). These findings were concordant with prior findings that the mothers of diabetic children were more depressed and anxious than the mothers of control children.

Conclusion: Though there are several limitation to this study, this study replicate prior findings supporting the effect of chronic disease .

References:

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NR67 Monday, May 22, 9:00 AM - 10:30 AM

Association Between Polymorphic Variations in GABRA3 Gene and Suicide Attempts as a Stress Response

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand a genetic association study.

Summary:

Introduction: Data from current research support the association between polymorphic variations in Gamma-aminobutyric acid -A receptor genes with specific personality characteristics or physiological responses to psychological stress (Uhart M et al. 2004). As stress almost always precedes suicidality (van Praag HM 2004), polymorphic variations in Gamma-aminobutyric acid -A receptor genes should be associated with suicide attempts.

Methods: Our workgroup has conducted a genetic association study between suicide attempts and the polymorphic variations of GABRA3 gene, located in chromosome X. The subjects consisted of 371 suicide attempters (66% women and 34% men) admitted in the emergency room of *Ramón y Cajal Hospital* in Madrid (Spain). Suicide attempts were defined according to the National Institute of Mental Health. Suicide attempts as a stress response were assessed with the St. Paul-Ramsey Life Events Scale. All cases were evaluated within 48 hours after the suicide attempt.

DNA for genotyping was extracted from a 10-ml blood sample according to standard methods. GABRA3 dinucleotide repeat polymorphism was studied by PCR amplification using primers previously described (Hicks et al. 1991). Allele and genotype frequencies were compared between groups using chi-square tests.

Results: Genotype *(a2)(allele 167)* was overrepresented in the male sample of suicide attempts non-related to a stressful event: 28,6% versus 7,8% in the overall male sample and 0% in the stress-related suicide attempts male sample (χ^2=13,466; df=3; p<0,05). We found no differences in the female sample.

Conclusions/Discussion: The present study suggests an association between allele *(a2) (167)* and suicide attempts in males. The suicide attempt in men with that particular genotype will not be a stress response and it will occur without a stressful event prior to the attempt. Our results may be biased by the sample size and the low prevalence of the allelic variant studied. Future studies should replicate our work with lager samples to confirm the results.

References:

1. Uhart M, McCaul ME, Oswald LM, Choi L, Wand GS. GABRA6 gene polymorphism and an attenuated stress response. Mol Psychiatry 2004; 9(11):998-1006.
2. Hicks AA, Johnson KJ, Barnard EA, Darlison MG. Dinucleotide repeat polymorphism in the human X-linked GABAA receptor alpha 3-subunit gene. Nucleic Acids Res 1991; 19: 4016.

NR68 Monday, May 22, 9:00 AM - 10:30 AM

A Seminal Articles Course Developed and Led by a Resident

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Educational Objectives:

To demonstrate the effectiveness of a resident organized and led course on noteworthy articles, both psychodynamic and psychopharmacologic, that was directed at potentially broadening residents' exposure to journal based learning. To illustrate the issues in the execution and outcome evaluation of such a course, that utilized a syllabus, resident instructor, and rotating faculty facilitator for engendering lively discussion.

Summary:

Objective: A Seminal Articles Course was developed by a resident for twenty-seven psychiatric residents at the Maimonides Medical Center to ascertain whether improved attendance and clinical learning would occur from a revised journal club focusing on landmark articles.

Method: Thirteen classic or controversial psychodynamic and psychopharmacologic articles were selected from a list of sixty articles obtained through faculty inquiry and Medline searching. The course consisted of a syllabus and thirteen lectures led by both a resident instructor and a rotating faculty facilitator. Each lecture involved a summary of the article, a review of the topic, and discussion time. Evaluations were filled out after each session and at the end of the course.

Results: Major issues involved in developing the course were 1) arranging the course's logistics, 2) establishing the thirteen articles to be reviewed, 3) obtaining commitments from the participating faculty, 4) organizing the content of the lectures, and 5) developing the evaluation instruments. The course had an average attendance of 70%, which is equivalent to that seen for other popular courses. There was an 86% return rate for the evaluations. The same average rating of 92% was given concerning the content of the articles, the adequacy of the resident instructor, and the clarity of the faculty facilitators. Residents graded the clinical usefulness of the overall course with a rating of 89% and the effectiveness of the course's teaching method with a rating of 87%.

Conclusion: Residents indicated through their attendance and evaluations that the course was worthwhile and useful. Residents gained from the variety of the articles used, the diversity of the instructors, and the ample discussion time. The resident organizer gained from the teaching experience an appreciation of the time and process involved in developing such a course.

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NR69 Monday, May 22, 9:00 AM - 10:30 AM

The Effect of Attention Deficit on Executive Function in Patients With Traumatic Brain Injury

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Educational Objectives:

According to the stage model(Saccuzzo & Braff, 1981), attention deficits that is basic stage in information processing lead to memory disturbance(Green, 1999) and subsequently affect higher-order cognitive function such as decision-making, abstract thinking, and judgement related to executive function(Green, 1993).

The purpose of this study was to investigate the effect of cognitive function on executive function in Traumatic Brain Injury(TBI) patients.

Summary:

Objectives: The purpose of this study was to investigate the effect of cognitive function on executive function in Traumatic Brain Injury(TBI) patients.

Methods:

(1) Participants: Participants were 122 patients(high executive function group: 52, low executive function group: 70) who first were presented with Traumatic Brain Injury to a university hospital referred to a TBI clinic.

(2) Measures: i) Korean-Wechsler Adult Intelligence Scale, ii) Executive Intelligence Test(EXIT: Kim, 2001): this test measure attention(Stroop test), language(Word fluency), memory(Rey AVLT), and visuospatial(Design fluency) function related to executive function.

(3) Procedure: Participants were divided into two groups according to EXIT score, which of high function group was more than 80(above low average) and of low function group was under 80(under borderline). Seventy low function group(age: M=41.63, SD=11.34) was compared with fifty two high function group(age: M=38.12, SD=12.06). Using hierarchical regression analysis, EXIT score(EIQ) was regressed on 4 subscales after controlling for IQ.

Results:

(1) The difference of IQ between low and high function group

A Student's t-test showed that low function group's mean score of IQ(M=84.58; SD=11.18) were significantly lower than low function group's(M=98.65; SD=12.53), $t(117)=-6.46$, $p<001$. Because of being this difference between two groups, we examine (2) the effect of cognitive function on executive function in two groups after controlling for IQ:

In the low function group, only attention($\beta=.22$, $p<.05$) predicted significantly EIQ, indicating that lower attention were related to lower EIQ after controlling for IQ. In the high function group, only memory($\beta=.31$, $p<.01$), indicating that lower memory were related to lower EIQ.

Conclusion:

Only attention was positively related to executive function, in TBI patients with low executive function. Whereas, in TBI patients with high executive function, memory was positively related to executive function than other cognitive function. It is concluded that executive dysfunction is caused by attention deficits.

References:

1. Green P, Iverson GL, Allen L.:Detecting malingering in head injury litigation with the Word Memory Test. Brain Inj. 1999; 13(10):813-9.
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NR70 Monday, May 22, 9:00 AM - 10:30 AM

Comparison Between Subjective and Actigraphic Measurement of Sleep in Psychiatric Inpatients

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that objective sleep measurement is needed to evaluation sleep parameters in psychiatric inpatients with severe depression or anxiety due to more discrepancies between subjective and objective assessment of sleep. And also this presentation showed that sleep parameters in the patients who reported poor sleep quality should be evaluated using objective measures.

Summary:

Objectives

Patients with psychiatric disorders commonly complain about sleep disturbance. Assessment of sleep disturbance is an essential part of the diagnostic criteria used for several psychiatric disorders. Clinically, psychiatrists depend on subjective report when

they evaluate quality of sleep in psychiatric inpatients. This study aimed to compare subjective assessment with actigraphic measurement of sleep.

Methods

A total of 32 psychiatric inpatients were recruited. Patients were asked to wear a wrist actigraphy for three consecutive days and to fill out a sleep diary each morning. The severity of depression and anxiety was evaluated according to Beck Depression Inventory and State-Trait Anxiety Inventory. Subjective satisfaction about quality of sleep was also evaluated according to visual analog scale for three days. Nurses assess sleep at every night rounding for three days.

Results

There is statically significant difference of sleep latency between patient's sleep log and actigraphic measurement. Nurses's report are more consistent with actigraphic measurement than patients' sleep log. Interestingly, subjectively poor sleepers show no significant difference of sleep parameters comparing with good sleepers. Subjectively poor sleepers report their sleep latency longer than actigraphic assessment. The discrepancy between subjective and actigraphic measurement of sleep latency significantly correlated with severity of anxiety and depression.

Conclusions

Nurses tend to overestimate sleep while patients tend to underestimate their sleep. Objective sleep measurement is needed to evaluation sleep parameters in psychiatric inpatients with severe depression or anxiety due to more discrepancies between subjective and objective assessment of sleep. And also this presentation showed that sleep parameters in the patients who reported poor sleep quality should be evaluated using objective measures.

References:

1. Lockley SW, Skene DJ, Arendt J: Comparison between subjective and actigraphic measurement of sleep and sleep rhythms. J Sleep Res 1999; 8:175-83.
2. Tsuchiyama K, Nagayama H, Kudo K, et al.: Discrepancy between subjective and objective sleep in patients with depression. Psychiatry Clin Neurosci 2003; 57:259-64.

NR71 Monday, May 22, 9:00 AM - 10:30 AM

Polymorphisms in Catechol-O-Methyltransferase and Monoamine Oxidase-A Genes and Homicidal Behaviors in Schizophrenia

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the associatoin of functional polymorphisms of COMP and MAO-A with schizophrenia patients who committed homicide as a extreme case of aggressiveness.

Summary:

Recent studies have shown that functional polymorphisms of catechol-O-methyltransferase(COMT) and MAO(MAO) genes are associated with the aggressiveness in schizophrenic patients. The purpose of the present study was to assess the associations of functional polymorphisms of COMT and MAO-A with schizophrenia patients who committed homicide as a extreme case of aggressiveness.

92 schizophrenic patients who committed homicide, 95 schizophrenic patients who has never commited homicide participated in this study. Diagnostic evaluation was made with SCID(Structured Clinical Interview for DSM-IV), and history of suicide attempts was evaluated also. Val158Met and Ala72Ser functional polymorphisms of COMT and VNTR polymorphism of MAO-A was analysed.

There were significant difference in genotype distribution(GG : GA/AA) of Val158Met polymorphism(P=0.04) and in allele frequency(G : T) of Ala73Ser polymorphism(P=0.045). But, no significant results was found in VNTR polymorphism of MAO-A gene(P= 0.74). There were no significant results in genotype distribution and allele frequencies of two functional polymorphisms of COMT gene, VNTR distribution of MAO-A gene when performed subgroup analysis by the existence of history of suicide attempts.

Low activity of COMT is associated with aggressiveness in schizophrenia was repeatedly reported by many authors. We confirmed the association of low enzyme activity of COMT gene with the aggressiveness of schizophrenia, but not with MAO-A gene. But, history of suicide attempt-the aggressivness to self- was not associated with the enzyme activity of COMT and MAO-A gene.

Key Words : Schizophrenia, homicide, suicide, COMT, MAO-A

References:

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NR72 Monday, May 22, 9:00 AM - 10:30 AM

Predictors of Bipolar Disorder Risk Among Patients Currently Treated for Major Depression

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Educational Objectives:

To identify predictors of bipolar disorder risk among patients currently in treatment for major depression disorder.

Summary:

Objective: This study sought to identify predictors of bipolar disorder (BPD) risk among patients treated for MDD.

Method: Psychiatrists from community and private practice clinic settings randomly selected patients who demonstrated one or more antidepressant (AD) medication failures during the current episode of MDD. Patients with BPD, OCD, or schizophrenia were excluded. Patient history and AD use were obtained via record abstraction. Patients self-reported their demographics, family history, co-morbid health status, alcohol/drug use, legal problems, and current depression symptoms via Centers for Epidemiologic Studies - Depression (CES-D) scale. BPD screening was self-reported via the Mood Disorder Questionnaire (MDQ.

Results: For n=602 patients the base MDQ positive rate was 18.6%. Stepwise logistic regression identified five variables associated with bipolar disorder risk (MDQ+): The CESD item "people were unfriendly" (OR=2.59, p<.001), co-morbid anxiety (OR=2.98, p<.002), depression diagnosis within five years (OR=2.47, p<.001), family history of BPD (OR=2.01, p<.010), and legal problems (OR=1.74, p<.026). For patients with no risk factors (n=41) 2.4% were MDQ+. For patients endorsing "people were unfriendly" (n=103), 31.1% were MDQ+; adding co-morbid anxiety (n=82) increased MDQ+ rate to 35.4%; adding recent depression onset (n=17) increased MDQ+ rate to 41.2%; adding family history (n=4) increased MDQ+ rate to 75%; 100% of those endorsing all 5 factors (n=3) were MDQ+. For patients endorsing any three or more risk factors (n=109) 41.3% were MDQ+.

Conclusions: Over one-third of patients who experienced projection or rejection sensitivity via endorsement of the CESD item "people were unfriendly" as well as co-morbid anxiety, were at risk for BPD (MDQ+). These two clinical features and recent depression onset, BPD family history and legal problems may prove useful indicators of BPD risk among patients with difficult to treat depression.

Research supported by GlaxoSmithKline.

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NR73 Monday, May 22, 9:00 AM - 10:30 AM

Effectiveness of Lamotrigine in a Clinical Setting

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Educational Objectives:

recognize that lamotrigine appears effective in bipolar disorder patients in a clinical setting, with a low discontinuation rate and commonly not requiring subsequent additional pharmacotherapy

Summary:

Objective: To assess the effectiveness of lamotrigine in bipolar disorder (BD) patients in a clinical setting.

Method: Open lamotrigine was naturalistically administered to BD outpatients assessed with the Systematic Treatment Enhancement Program for BD (STEP-BD) Affective Disorders Evaluation, and followed with the STEP-BD Clinical Monitoring Form.

Results: 169 BD (55 type I, 98 type II, 16 NOS) patients (mean age 42.0±14.3 years, 64% female) taking a mean of 1.9 other psychotropic prescription medications received lamotrigine for a mean duration of 382±380 days, with a mean final dose of 236±144 mg/day. Only 44/169 (26%) patients discontinued lamotrigine; 12/169 (7%) for inefficacy, 6/169 (4%) for benign rash, 5/169 (3%) for nonadherence, and 21/169 (12%) for other reasons. 91/169 (54%) patients taking lamotrigine required subsequent additional pharmacotherapy; 39/169 (23%) for anxiety/insomnia, 28/169 (17%) for depressive symptoms; 19/169 (11%) for manic/hypomanic/mixed symptoms, and 5/169 (3%) for weight control. Mean time to addition of another psychotropic in these patients was 129±115 days. Thus, 54/169 (32%) continued lamotrigine with no subsequent psychotropic added (lamotrigine duration 271±347 days), 71/169 (42%) continued lamotrigine, but had subsequent psychotropic added (added subsequent psychotropic at 133±124 days, lamotrigine duration 562±414 days), and 44/169 (26%), discontinued lamotrigine (lamotrigine duration 227±208 days).

Conclusion: Lamotrigine had a low (26%) discontinuation rate and patients commonly did not require subsequent additional pharmacotherapy, suggesting effectiveness in a clinical setting.

Supported by GlaxoSmithKline.

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NR74 Monday, May 22, 9:00 AM - 10:30 AM

Efficacy of ECT in Treatment Resistant Patients With Mental Illness: Naturalistic Study

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Educational Objectives:

"At the end of my presentation, the participants should be able to recognise the significant efficacy of Electroconvulsive therapy (ECT) even in treatment resistant severe depressive disorders."

Summary:

INTRODUCTION: The use of ECT, an effective treatment for MDDs, has been declined in the United Kingdom (UK) over the years except for severe treatment resistant cases. It was, therefore, sought to assess whether the efficacy of ECT is still high in such a severely affected population.

METHODS: It was a naturalistic observational study over a period 18 months including every patient referred for ECT at the local psychiatric hospital. Each participant was subjected to a battery of clinical and cognitive tests before the start, in the middle, at the end and 3 months after course of ECT treatment. In addition, ratings on depression were performed weekly during the treatment. The main outcome measure was the 24-item version of the Hamilton Depression Rating Scale (HAMD).

RESULTS: We analysed the results of patients who had ECT primarily for depression, had at least 6 sessions or less if achieved remission earlier, and had at least 21 points on the HAMD before the treatment. There were 31 patients satisfying these criteria, 12 male and 19 female. Among them 20 (65%) had positive family history in a first-degree relative and18 (58%) had psychotic features. All of them except two had not only been classified as treatment resistant according to standard criteria but had also received at least one augmentation treatment such as lithium, atypical antipsychotics, thyroid hormones etc. The majority of patients received bilateral treatment (24 of 31) and a mean of 8.9 ECT sessions. Their HAMD scores improved from an initial 33.1 to 13.6: a 59% improvement. A remission (HAMD<10) was achieved by 16 patients (52%).

CONCLUSIONS: Despite that ECT is reserved only for the most severely ill patients in UK; it is still highly effective with achieved remission in 52% of patients as in this study.

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NR75 Monday, May 22, 9:00 AM - 10:30 AM

Quetiapine as Treatment of Non-Psychotic Unipolar Depression With Residual Symptoms: Double Blind, Randomized, Placebo Controlled Study

Atul Khullar, M.D. *University of Alberta, Psychiatry, 106 Erie Street South, Devon, AB, T9G 1A7, Canada*, Pratap Chokka, M.D., Danielle Fullerton, M.S.C., Shelley McKenna, R.N., Adam Blackman, M.D.

Educational Objectives:

1. Consider the major evidence pointing towards possible antidepressant effects of quetiapine.
2. Briefly evaluate a pilot study showing the potential effectiveness of quetiapine as an adjunctive treatment to SSRI/SNRI agents in non-psychotic unipolar depression.
3. Speculate on the overall clinical utility of the quetiapine as a treatment of non-psychotic depressive symptoms in clinical practice.

Summary:

Introduction: New studies indicate the benefit of quetiapine in the depressive phase of bipolar disorders (1). An emerging body of literature is also demonstrating the potential effectiveness of quetiapine as adjunctive treatment in non-psychotic unipolar depression (NPUD) (2). To our knowledge, there is no published controlled trial data in this area for quetiapine, which is frequently used as an augmentation agent in NPUD.

Methods: 16 patients with a current DSM-IV major depressive episode without psychotic features (diagnosed by the MINI) who had residual symptoms (HAMD > 16) after at least 6 weeks of treatment with an adequate dose of SSRI/SNRI were randomized into placebo and flexibly dosed (100-600mg once daily) quetiapine groups for 8 weeks. 1 patient was dropped for stopping venlafaxine prior to receiving treatment.

Results: A LOCF analysis (n=15) using independent samples t-tests demonstrated significantly greater ($p<.05$) mean changes in the HAMD17 (11.875 versus 4.86, p =.018), MADRS (14.88 versus 5.29, p=.007), HAM-A (11 versus 4.14, p=.007) for the quetiapine group (n=8) versus the placebo (n=7) group. Trends towards significance were seen in the PSQI (6.00 versus 3.28, p=.136), SDS (7.18 versus 1.93, p=.11) and CGI-S (1.38 versus .57, p=.063) for the quetiapine group. There were no significant differences in CGI-I, weight gain and measures of cholesterol/glucose between groups. 3 of 8 patients in the quetiapine group remitted (HAMD17 <7) versus none in the placebo group. The average dose of quetiapine in the treatment group was 350mg.

Conclusions: This study demonstrated the potential use of quetiapine as an adjunctive treatment for depression with residual symptoms. Limitations of this study include the small sample size and no prospective determinant of residual depressive symptoms. However, these promising results indicate a need for larger scale controlled trials in this area.

Research supported by the Investigator initiated trials program from Astra Zeneca

References:

1. 1. Calabrese JR, Keck PE Jr, Macfadden W, Minkwitz M, Ketter TA, Weisler RH, et al: A randomized, double-blind, placebo-controlled trial of quetiapine in the treatment of bipolar I or II depression. Am J Psychiatry 2005;162(7):1351-60.

2. 2. Barbee JG, Conrad EJ, Jamhour NJ: The effectiveness of olanzapine, risperidone, quetiapine, and ziprasidone as augmentation agents in treatment-resistant major depressive disorder. J Clin Psychiatry 2004;65(7):975-81.

NR76 Monday, May 22, 9:00 AM - 10:30 AM

An Interaction Between the Serotonin Transporter Promoter Region and Dopamine Transporter Polymorphisms Contributes to Harm Avoidance and Reward Dependence Traits in Normal Healthy Subjects

Sang-Joon Son, M.D. *Seoul*, Se-Joo Kim, M.D., Hong-Shick Lee, M.D., Chan-Hyung Kim, M.D.

Educational Objectives:

These findings suggest that the variants of *5-HTTLPR* interacted with the *DAT1* gene polymorphism to influence the HA and RD temperament subscales of TCI. Neither of these two genes affected any subscales of TCI alone.

Summary:

There is evidence for an association between polymorphisms of 5HT- and dopamine-related genes and temperamental personality traits. Recent findings have shown that interactions between allelic variants of the different genes may contribute to personality traits. We examined the effects of 5HT transporter-linked promoter region (*5-HTTLPR*) and dopamine transporter (*DAT1*) gene polymorphisms for associations with the Temperament and Character Inventory (TCI) temperament subscales in 209 Koreans. Controlling for the effects of gender and age, we found significant interactions between *5-HTTLPR* and *DAT1* genes on Harm Avoidance (HA) and Reward Dependence (RD) as measured by the TCI (Hotelling's Trace = 3.0, P=0.02). In the presence of the *DAT1* 10/10 genotype, subjects of group L of *5-HTTLPR* had a significantly higher HA score and significantly lower RD score than those of group S (F=5.04, df=1, p=0.03 and F=2.30, df=1, p=0.14, respectively).

These findings suggest that the variants of *5-HTTLPR* interacted with the *DAT1* gene polymorphism to influence the HA and RD temperament subscales of TCI. Neither of these two genes affected any subscales of TCI alone.

References:

1. Benjamin J (1998) Genes for human personality traits. Sci Context 11(3-4):357-372.
2. Cloninger CR (1986) A unified biosocial theory of personality and its role in the development of anxiety states. Psychiatr Dev 4:167-226.

NR77 Monday, May 22, 9:00 AM - 10:30 AM

One-Year Naturalistic Study of Patients With Panic Disorder

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the outcome predictor of panic disorder

Summary:

Objective: Only a few prospective studies of panic disorder are available. This study investigated naturalistic outcome of panic disorder patients at 12 months after the initial diagnosis.

Method: A total of 84 subjects were diagnosed with panic disorder by initial diagnostic interview with a psychiatrist, Structured Clinical Interview for DSM-IV (SCID-IV) and Anxiety Disorder Interview Schedule for DSM-IV (ADIS-IV). Among them, 80 subjects could be evaluated by means of Panic Disorder Severity Scale (PDSS) at intake interview and follow-up interview after 12 months. Treatment continuation was also examined at follow-up interview.

Results: At initial intake, 80 patients were classified into 21% with mild, 35% with moderate-to-marked, and 44% with severe symptoms on the basis of their PDSS total score. After 12 months, 20% of patients reached remission, 65% had mild and 15% had moderate-to-marked symptoms. Initial panic symptom severity, presence of agoraphobia, panic symptom duration before diagnosis, number of comorbid Axis I disorders were associated with significantly high PDSS total score 1 year after. 44% of total patients continued medication and 26% have stopped treatment by

clinician's recommendation and 30% have self-discontinued their medication. 1 year later, all three groups were improved but self-discontinuation group had significantly high panic disorder severity score.

Conclusion: In the 1 year naturalistic outcome study of panic disorder patients, a high percentage of patients achieved remission or had mild symptoms. Poorer outcome was predicted by initial severity, agoraphobia, longer duration before diagnosis, an increasing number of comorbid Axis I disorders and early treatment discontinuation.

References:

1. Dannon PN: Three year naturalistic outcome study of panic disorder patients treated with paroxetine. BMC Psychiatry 2004; 4:16.

2. Toni C: Spontaneous treatment discontinuation in panic disorder patients treated with antidepressants. Acta Psychiatr Scand. 2004: 110:130 137.

NR78 Monday, May 22, 9:00 AM - 10:30 AM

Decreased Plasma Antioxidant Levels in Patients With Dementia From Alzheimer

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Educational Objectives:

Objectives : Previous studies have explained one of the pathophysiologic mechanism of dementia of Alzheimer's type by oxidative damage to the neuron. This study compare the representative plasma antioxidants (albumin, total bilirubin, uric acid) level between normal controls and patients with dementia of Alzheimer's type.

Summary:

Objectives : Previous studies have explained one of the pathophysiologic mechanism of dementia of Alzheimer's type by oxidative damage to the neuron. This study compare the representative plasma antioxidants (albumin, total bilirubin, uric acid) level between normal controls and patients with dementia of Alzheimer's type.

Methods : Excluded due to nutritional unbalance or medico-surgical problem by physical exam and laboratory test, the remainder Alzheimer's patients are 102 people (male 42, female 60) and remainder normal controls are 99 people (male 47, female 52). Plasma antioxidants level are compared between the two groups.

Results : Compared with covariate of age and sex, all plasma antioxidants level are significantly lower in patients with dementia of Alzheimer's type than in normal controls. albumin ($F=36.179$, $p<0.001$), bilirubin ($F=101.508$, $p<0.001$), uric acid ($F=12.688$, $p<0.001$). Additionally, compared between the plasma antioxidants level and the scores of MMSE in the patients with dementia of Alzheimer's type adjusted for age and sex, only plasma albumin level shows positive correlation with the scores of MMSE ($p=0.017$). And there is no correlation between the plasma antioxidants level and the brain atrophic change respect to brain MRI.

Conclusion : This study presents that plasma antioxidants level are lower in the patients with dementia of Alzheimer's type than normal elderly controls and this results correspond to oxidative neuronal damage in dementia of Alzheimer's type.

References:

1. Barberger-Gateau P, Fabrigoule C, Helmer C, Rouch I,.

2. Barrett-Connor E, Edelstein SL, Corey-Bloom J, Wiederholt.

NR79 Monday, May 22, 9:00 AM - 10:30 AM

Psychological Characteristics in Remission State Schizophrenia Patients With The PAI

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to predict patient's prognosis and give proper treatments to schizophrenic patients as each patient's phase of illness.

Summary:

Background

The prevalence of depression, anxiety and other psychological symptoms are highly reported in schizophrenic patients during different phase of schizophrenia.

Aims

The purpose of this study was to assess psychological problems and symptoms of Patients with Schizophrenia during remission stage. We divided schizophrenic patients into two subgroups whether they had auditory hallucination during their acute phase or not. The aim was to explore relationship between the remission stage phenomenological features and acute phase psychotic symptoms.

Method

Personality Assessment Inventory (PAI, Morey, 1991) was administered to 30 patients with a DSM-IV diagnosis of paranoid schizophrenia and 60 control subjects. Patients with Clinical Global Impression (CGI, Guy, 1976) severity scale score of ≤ 3 were enrolled in remission group the patients. 16 out of 30 patients were reported they experienced auditory hallucination during their acute phase whereas 14 out of 30 patients were not reported.

Result

The somatic complaints scale was significantly high in the subgroup of patients with auditory hallucination during their acute phase compared to the non-auditory hallucination group. However, the non-auditory hallucination group had significantly higher scores on the depression, anxiety and social withdrawal scale than auditory hallucination group.

Discussion

Nevertheless schizophrenic patients are released from their acute psychosis, patients still have psychological issues to be treated. Furthermore, during the remission period, patients who have delusion but not auditory hallucination and patients who have both might have different psychological aspect.

References:

1. Morey LC: The Personality Assessment Inventory Professional Manual, Odessa, FL, Psychological Assessment Resources, 1991.

2. Guy W, ECDEU Assessment for Psychopharmacology, Revised Edition, Rockville, MD, NIMH Publication, 1976.

NR80 Monday, May 22, 9:00 AM - 10:30 AM

Which Variables are Related to Quality of Life of Patients With Traumatic Brain Injury?

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Educational Objectives:

At the conclusion of this presentation, the participants should be able to recognize how to approach mild to moderate traumatic brain injury patients to improve their quality of life

Summary:

Objective: One of the goals in the rehabilitation program of TBI patients is to improve Quality of life(QOL) including subjective satisfaction. This study investigated which variables were related to QOL in TBI patients and it would be differed by findings of brain MRI(MRI).

Method: 39 patients who have complained decreased cognitions, affective symptoms and personality changes after mild to moderate TBI were recruited. 22 patients have shown abnormal brain MRI findings correlated with their injury and 17 patients have normal brain MRI findings. Patients were assessed by using Hamilton rating scale for depression(HAMD), Hamilton anxiety scale(HAMA) and Functional assessment scale(FAS). All patients also have completed Symptom check list(SCL-90-R), Beck depression inventory(BDI), State-trait anxiety inventory(STAI), Korean version of the SmithKline Beecham 'Quality of Life' scale(Kv-SBQOL) and Marlowe-Crown Social Desirability Scale(MCSDS). In addition, Korean Wechsler Adult intelligence Scale (K-WAIS), Rey-Kim Memory Scale(R-KMS), Kims Frontal-executive neuropsychological test(KF-ENT) were assessed. We conducted partial correlation and stepwise regression analysis using SPSS version 11.0.

Results: The scores of QOL were significantly correlated with FAS($p<0.05$), several subscales of SCL-90-R(obsessive-compulsive($p<0.05$), depression($p<0.05$), anxiety($p<0.05$), global severity index($p<0.05$) and positive symptom total($p<0.05$)) after controlling for MCSDS. However, in normal MRI finding group, those were significantly correlated with STAI, BDI, all subscales of SCL-90-R($p<0.05$).

In stepwise regression analysis, positive symptom total($p<0.01$) and interpersonal sensitivity($p<0.01$) subscales of SCL-90-R could explain 62.1 % and 10.9% of the variance of the QOL score in patients with abnormal MRI findings. As for the patients with normal MRI findings, depression($p<0.01$) subscale of SCL-90-R accounted for 54.2% of that of the QOL score.

Conclusion: This finding suggests that subjective psychiatric symptoms including depression were significantly correlated with the subjective QOL of TBI patients in both groups. However, the patients with abnormal MRI findings should be additionally focused on the daily functioning to improve QOL.

References:

1. Eva Berger, Friederike Leven, Nicola Pirente, Bertil Bouillon and Edmund Neugebauer: A systemic review of the literature: Quality of life after traumatic brain injury. Restor Neurol Neurosci 1999; 14:93-102.
2. Mark V. Johnston, PhD, Yael Goverover, PhD, OT, Marcel Dijers, PhD: Community Acitivities and Individuals' Satisfaction with them: quality of life in the first year traumatic brain injury. Arch Phys Med Rehabil 2005; 86:735-745.

NR81 Monday, May 22, 9:00 AM - 10:30 AM

Association Of Streptococcal Infections With OCD in Pedigrees

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the possible association between streptococcal infections and obsessive-compulsive disorder.

Summary:

Background: Clinical studies suggest a pathological link between Group A Streptococcus (GAS) infections and obsessive compulsive/tic symptoms. While previous reports suggest a genetic model of inheritance in OCD, few published reports have examined the heritability of streptococcal-associated OCD.

Methods: We examined 46 family members in a five-generation pedigree with high rates of both streptococcal infections and OCD. Interviews were conducted in person by psychiatrists and/or students. Obsessive-compulsive severity was assessed by the Yale-Brown Obsessive Compulsive Scale (Y-BOCS), or Child Y-BOCS (CY-BOCS). Diagnoses of lifetime OCD were made by a psychiatrist. The number of streptococcal infections per patient was verified through medical records. Three distinct groups were identified: positive streptococcal history without OCD, positive streptococcal history with OCD, and those without streptococcal histories or OCD. A positive streptococcal history was defined as 2 or more infections within 2 years, streptococcal infections leading to tonsillectomy, or a "complicated" streptococcal infection resulting in rheumatic fever.

Results: 18 patients met lifetime criteria for OCD and had positive streptococcal infection histories. All patients with OCD diagnoses were found to have positive streptococcal histories. The average YBOCS score for these subjects was 17 ($\pm$7.5). 7 subjects were found to have positive streptococcal histories without OCD and 21 subjects did not meet criteria for OCD or a positive streptococcal history. The risk (and 95% confidence interval) of having an OCD diagnosis for those with positive streptococcal histories was found to be 72.0% (52.2%, 85.7%). The odds (and 95% confidence interval) of an OCD diagnosis for those with a positive streptococcal history was found to be 2.57 (1.10, 6.00).

Conclusions: These preliminary results suggest that the susceptibility to OCD onset following multiple streptococcal infections may be a heritable trait.

References:

1. Swedo SE: Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS). Mol Psychiatry 2002;7 Suppl 2:S24-5.
2. Mell LK, Davis RL, Owens D: Association between streptococcal infection and obsessive-compulsive disorder, Tourette's syndrome, and tic disorder. Pediatrics 2005; 116(1):56-60.

NR82 Monday, May 22, 9:00 AM - 10:30 AM

Depression and Anxiety Among Toronto School-Aged Children

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Educational Objectives:

At the conclusion of this session, the participant should know the prevalence of depression and anxiety syndromes in a Toronto based community sample of urban children in Grades 3 through 6.

Summary:

The purpose of this study was to describe depression and anxiety rates in a community sample of 680 (49.5% female, 50.1% male) urban Toronto children Grades 3 to 6 using the Children's Depression Inventory (CDI) and the Multidimensional Anxiety Scale for Children (MASC). Previous Canadian epidemiological studies (Bretton et al., 1999; Fleming et al., 1989) covered a range of populations, yet results might not apply to the fast-growing and extremely diverse Toronto school-aged child population. Descriptive, secondary data analyses were conducted using information collected as part of a larger prevention study. On the CDI, 5.6%

of children fell within the clinical range and 16.9% in the sub-clinical range. Unlike previously reported gender distributions for depressed preadolescents, 65.8% of those in the clinical range were females. Of those who were clinically depressed children, 24.3% had a comorbid clinical anxiety. On the MASC, 7.8% fell within the clinical range and 9.6% in the sub-clinical range (66>t>60). No sex differences in anxiety rates were found. Of MASC subscales, separation anxiety was significantly elevated most often (32.4%) for clinically depressed. Compared to previous research, similar rates of depression and anxiety were found. Unique to the current research were differences in gender distribution and comorbidity.

References:

1. Bretton JJ, Bergeron L, Valla JP, Berthiaume C, Gaudet N, Lambert J, and others: Quebec Child Mental Health Survey: Prevalence of DSM-III-R Mental Health Disorders. J Child Psychology and Psychiatry 1999; 40:375-384.
2. Fleming JE, Offord DR, Boyle MH: Prevalence of childhood and Adolescent depression in the Community ' Ontario Child Health Study. British J Psychiatry, 1989; 155:647-654.

NR83 Monday, May 22, 9:00 AM - 10:30 AM

Affective Processing in a Major Depressive Episode: fMRI Investigation in Bipolar Disorder and MDD

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Educational Objectives:

1. To delineate similarities and differences in regional brain activity during affective processing during a major depressive episode (MDE) in subjects with BD and major depressive disorder MDD (state-effects).
2. To characterize similarities and differences in the fMRI profile of response to identical pharmacotherapy amongst BD and MDD (treatment effects).
3. To compare differences in regional brain activity mediating affective processing in remitted subjects with mood disorders (BD and MDD subjects) to psychiatrically unaffected volunteers (trait-effects), and to contrast these trait-specific changes in BD and MDD subjects

Summary:

Background: Functional MRI technology provides an opportunity to delineate/elucidate putative neural circuits which are the substrate of emotional expression and affect regulation. Hitherto, there have been no investigations employing this technology in both major depression and bipolar depression along with a healthy control group.

Methods: To delineate similarities and differences in regional brain activity during affective processing during a major depressive episode (MDE) medication-free subjects who meet criteria for a major depressive episode in the context of BD (n=15) or MDD (n=15), and a group of psychiatrically unaffected control subjects (CS, n=15), underwent a mood challenge under fMRI scanning conditions.

Results: Both BD and MDD subjects receive olanzapine (Olanzapine®) - fluoxetine (Fluoxetine®) combination therapy to treat an MDE, with additional fMRI data acquisition at 1, 3, and 6 weeks following pharmacotherapy initiation. During the imaging session, visual affective stimuli is presented in two runs. In the first run blocks of neutral and positive valence pictures, are presented, while the second run consists of alternating neutral and negative blocks. Preliminary clinical and neuroimaging results from the first 12 subjects (MDD and BD) is presented.

Conclusions: Mood induction paradigm was successful in eliciting changes in self-rated affect. Changes were observed in regional brain activity in response to both positive and negative affect. Additionally, changes were observed between HC and MDD groups at baseline, with additional changes observed longitudinally in MDD group associated with improvements in depressive symptoms.

References:

1. Davidson RJ, Irwin W, Anderle MJ, Kalin NH: The neural substrates of affective processing in depressed patients treated with venlafaxine. Am J Psychiatry 2003; 160(1):64-75.
2. Lawrence NS, Williams AM, Surguladze S, Giampietro V, Brammer MJ, Andrew C, Frangou S, Ecker C, Phillips ML: Subcortical and ventral prefrontal cortical neural responses to facial expressions distinguish patients with bipolar disorder and major depre.

NR84 Monday, May 22, 9:00 AM - 10:30 AM

The Relationship Between Memory Function and Executive Function in ADHD

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Educational Objectives:

Understaning the memory function and executive function in ADHD

Summary:

The objective in this study is to verify the relationship between memory and executive function in ADHD. At first, the memory functioning was compared between ADHD and normal children, and then the memory function in ADHD according to executive function level was compared. K-ABC, K-PIC, behavioral symptom checklists and the memory test (digit & visual span, verbal learning & visual recognition test) and executive function test (trail making test A, B & WCST) in computerized neurocognitive function test were performed on the 68 ADHD children and 30 normal children who had over the IQ 70. As results of comparing memory function between ADHD and normal children, forward span in verbal and visual span test ($p<.01$), delayed recall and total recall in verbal learning test ($p<.001$), and delayed recognition and total recognition in visual recognition test($p<.05$) showed significant difference. Comparing memory function between mild defected ADHD and severe defected ADHD, severe defected ADHD had lower memory function, especially in the total recall in verbal learning test. As result of that comparison, the factors affecting memory ability in ADHD were the spending time in trail making test, A & B, and preservative Extended Release rors in WCST. As conclusion, ADHD had lower memory function than normal children and memory function in ADHD was associated with the resistance to interference stimulus and cognitive flexibility

References:

1. Martinussen R, Hayden DC, Hogg-Johnson S, & Tannock R. A menta alanysis of working memory impairments in children with Attention-Ddeficit/Hyperacitivity Disorder. J AM ACAD Child Adolesc Psychiatry 2005; 44:4, 377-384.
2. Stevens J, Quittner AL, Zuckerman JB, Moore S. Behavioral inhibition, sel-regulation of motivation, and working momory in chilren with attention-deficit hyperactivity disorder. Dev Neuropsychologist 2002; 21: 117-139.

NR85 Monday, May 22, 9:00 AM - 10:30 AM

Depression and Health Related Quality of Life in Wait-Listed Patients Awaiting Dialysis Treatment

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Educational Objectives:

Health related quality of life (QoL) nowadays is becoming a frequently assessed outcome measurement. In healthier subgroup of chronic dialysed patients we found that psychological distress was a significant, independent and strong predictor of several quality of life domains.

Summary:

Depression is very prevalent in patients with end-stage renal failure. Previous studies focused mainly on non-selected dialysis patients with high co-morbidity and disease burden. We investigated a healthier subgroup of dialysis patients, who are waitlisted for renal transplantation, to assess the prevalence of depression. We also analyzed the association of depression with quality of life (QoL).

In a cross-sectional study, 214 waitlisted dialysis patients were enrolled. Participants completed a battery of self-administered, validated questionnaires, which included the Kidney Disease Quality of Life Questionnaire (KDQOL-SF^{TM}) and the Center for Epidemiologic Studies Depression (CES-D) scale. Laboratory data, basic socio-demographic characteristics were extracted from patients' charts.

82% of enrolled patients completed the CES-D scale. Mean age of the participant population was 48±12 years, 60% were males and 18% had diabetes. The prevalence of patients with depression was 41%. Patients with depressive symptoms were significantly older (52±11 versus 46±12 years; $p<0.01$). The average CES-D score was not significantly different between males and females (median[interquartile range] 11[13] versus 14.5[17] for males versus females, p=NS). Patients with depressive symptoms had significantly worse scores in several QoL domains (Burden of kidney disease: 59±22 versus 34±21; Sleep: 74±16 versus 54±16; Energy/fatigue: 68±21 versus 43±21; $p<0.001$ in all cases) than patients without depression. After adjusting for covariables (age, gender, serum albumin, serum hemoglobin, comorbidity, education, Kt/V), the CES-D score was a significant, independent predictor of most generic and disease specific QoL domains.

We found high prevalence of depression in dialysis patients awating renal transplantation. Psychological distress was a strong, independent predictor of quality of life in this patient population.
Grants: OTKA TS 040889, OTKA T038409, NKFP 1/002/2001, ETT 218/2003, TeT Foundation (2005/06, MN), Hungarian Eotvos Scholarship (MN).

References:

1. Kimmel PL, Peterson RA: Depression in end-stage renal disease patients treated with hemodialysis: tools, correlates, outcomes, and needs. Semin Dial. 2005;18:91-97.

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NR86 Monday, May 22, 9:00 AM - 10:30 AM

Gender Differences in Panic Disorder With Agoraphobia

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize gender differences in panic disorder with agoraphobia

Summary:

Objective: The goal of this study is determine the differences between male and female patients in terms of major clinical characteristics of panic disorder and agoraphobia. Method: The sample was consist of 116 patients with DSM IV diagnosis of panic disorder - 86 (74%) of women and 30 (26%) of men. The patients were examined by the various clinical instruments (The Hopkins Symptom Checklist, The Panic Appraisal Inventory, The Fear Questionnaire, The Beck Anxiety Inventory and The Beck Depression Inventory) in terms of examination of major clinical characteristics of the disorder before the beginning of the treatment. Results: Male and female patients did not differ significantly in the age of onset of panic disorder and agoraphobia (29.1±6.1 versus 30.9±8.4 years) and duration of panic disorder and agoraphobia (2.1±3.4 versus 3.0±3.5 years). Also, according to analysis of gender comparison by the certain clinical instruments, the results of the study show there were no statistically significant differences between male and female patients in the severity of depression, severity of overall anxiety, severity of (agora)phobia and cognitions related to panic disorder. Conclusion: The results of the study show there are no statistically significant gender differences in terms of major clinical characteristics of panic disorder and agoraphobia.

References:

1. 18. Starcevic V, Djordjevic A, Latas M, Bogojevic G: Characteristics of agoraphobia in women and man with panic disorder with agoraphobia. Depression and Anxiety 1998; 8: 8-13.

2. Bekker MHJ: Agoraphobia and gender: A review. Clin Psychol Rev 1996; 16:129-146.

NR87 Monday, May 22, 9:00 AM - 10:30 AM

Differences in Temperament and Character Inventory According to Dissociation Using Dissociative Experience Scale: Korean Version DES-K

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Educational Objectives:

The present investigation sought to explore individual differences in the dissociative experience. The Authors approach the question about whether this difference is nature or nurture. The participant should be able to recognize the meaning of individual differences.

Summary:

Objective:

There are individual differences in the dissociative experience. The Authors approach the question about whether this difference is nature or nurture. The present investigation sought to explore the relationship between personality trait and dissociation.

Method:

Seventy-nine Korean university students(16 males and 63 females) had completed DES-K(Dissociative Experience Scale-Korean version) to examine the ability of dissociation, Eye-roll Sign

which is suggested the biological marker of dissociative ability by Spiegel, and TCI-K(Temperament and Character Inventory-Korean version) in order to evaluate personality trait. We divided the students into two groups(high DES group≥20 and low DES group<20) to evaluate the differences in TCI-K.

Pearson's correlation test, t-test and regression analysis were used for statistical analysis.

Result:

1)In high DES-K group, score of self-directedness in TCI-K is higher than low DES-K group. There were statistically significant correlations between self-transcendence in TCI-K and amnesia subscale, absorbtion-imaginative involvement subscale in DES-K and total DES-K scale. Scores of self-transcendence in TCI-K was predicted for DES-K scores.

2)In high DES group, scores of Eye-roll Sign and squint subscale were higher than low DES group. There was no correlation between DES-K and Eye-roll Sign except weak correlation between depersonalization-derealization subscale in DES-K and gaze subscale in Eye-roll Sign.

3)There were statistically significant differences in Tellegan Absorbtion Scale-Korean version(TAS-K) and Natural Hypnotic Experiences Questionnaire(NHQ) between high DES-K group and low DES-K group. Also, there were statistically significant correlations between TAS-K and NHQ scale and DES-K.

Conclusion:

Although character dimension of TCI-K was related with dissociation, there was no difference in temperament dimension of TCI-K, and no correlation between DES-K and Eye-roll Sign. These results suggests that trait theory of dissociation is questionable and needs more investigations.

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2. Merckelbach H, Campo J, Hardy S, et al. Dissociation and fantasy-proneness in psychiatric patients : a preliminary study. Compr Psychiatry 2005 ; 46 : 181-5.

NR88 Monday, May 22, 9:00 AM - 10:30 AM

Dissociation of Working Memory From Decision-Making in Schizophrenia

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Educational Objectives:

At the conclusion of this presentation, the participants should be informed the OFC functioning of the schizophrenic patients is relatively uncompromised whereas their DLPFC functioning is compromised, and this supports the idea that different cortical areas mediate different cognitive tasks

Summary:

Purposes: The orbitofrontal cortex(OFC) has received particular attention in two cognitive domains: decision-making and reversal learning. The Iowa Gambling Task(GT) is an assessment tool, intended to simulate real-life decision-making processes believed to be associated with the OFC in the way it factors uncertainty, reward, and punishment. Using this task, we examined the performances of schizophrenia on GT and their relationships with other cognitive domains such as executive functions and intelligence.

Methods: Thirty-seven stable schizophrenic inpatients participated in this study. After providing written informed consent, they underwent clinical symptom assessments including the Positive and Negative Syndrome Scale, followed by IQ test, the GT and WCST. Thirty-seven normal controls were selected based on age and sex similarities to schizophrenia.

Results: There was no significant difference in the mean overall net score (advantageous minus disadvantageous deck selection) on GT performance between schizophrenic group and normal healthy controls. When it comes to chronological card choice in blocks of 20 cards, there were no significant main effects for group ($F1,72=3.08$, $p=.083$), and block($F4,72= .61$, $p=.65$) but a main effect for the group by block interaction was found($F4,72=2.96$, $p=.02$).

Not surprisingly, the schizophrenic patients completed significantly fewer categories and performed poorer in the other 4 indices than controls on the WCST. There were no significant correlations between Gambling Task and WCST.

Conclusions: This study examined the performance pattern on the GT in the schizophrenic patients, the result of which is still controversial. According to this study, one may infer that the OFC functioning of the schizophrenic patients is relatively uncompromised whereas their DLPFC functioning is compromised, and this supports the idea that different cortical areas mediate different cognitive tasks.

References:

1. Cavallaro R et al. Basal-corticofrontal circuits in schizophrenia and obsessive-compulsive disorder: a controlled, double dissociation study. Biol Psychiatry. 2003 Aug 15;54(4):437-43.
2. Rodriguez-Sanchez JM et al. Prefrontal cognitive functions in stabilized first-episode patients with schizophrenia spectrum disorders: a dissociation between dorsolateral and orbitofrontal functioning. Schizophr Res. 2005 Sep 15;77(2-3):279-88.

NR89 Monday, May 22, 9:00 AM - 10:30 AM

Quality of Life in Children With Developmental Disabilities and Their Families

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Educational Objectives:

At the conclusion of this presentation, the participants should be able to recognize the compromised quality of life in children with developmental disabilities, psychopathology, or other medical conditions. They should also understand that families of children with these conditions experience a substantial caring burden.

Summary:

Research on the quality of life (QOL) of children with developmental disabilities (DD) and their families is limited. It has, however, been reported that children with DD, such as autism and ADD/ADHD, have poorer adaptive functioning and are less independent than typically developing children. Analyzing data from National Survey of Children's Health, this study examined differences in QOL by comparing children with DD to children with other medical conditions and typical controls in the domains of social activity, family burden, family activities, schooling, and independence. Multivariate logistic regression was performed to compare each of the five case groups, autism (n=483), ADD/ADHD (n=6,319), learning disability (n=4,469), psychopathology (n=2,582), and other medical conditions (n=11,212), against typical controls (n=58,953) by three age strata (3-5, 6-11, and 12-17). All five case group families reported significantly higher child care burden than typical controls (p values all <.0001) across the three age strata. Case family members were more likely to stop working because of childcare issues (adjusted odds ratios (OR) ranged

from 1.49 to 5.27) than family members with typically developing children. Children in the five cases groups were also more likely to miss school or repeat a grade. Furthermore, children with autism, ADD/ADHD, and learning disabilities were significantly less likely than typical controls to participate in organized social activities, with the relative odds of participation consistently lowest for the autism group (ORs <0.50). No such effect was seen for children with other medical conditions or children with other psychopathologies. A reduced odds of organized social activity participation was seen only in the oldest age group. Findings from this analysis indicate that QOL for children with DD, psychopathology, or other medical conditions may be compromised and that the caring burden on families could be substantial.

References:

1. Sawyer MG, Whaites L, Rey JM, Hazell PL, Graetz BW, Braghurst P: Health-related quality of life of children and adolescents with mental disorders. J Am Acad Child Adolesc. Psychiatry 2002; 41:530-537.
2. Liss M, Harel B, Fein D, Allen D, Dunn M, Feinstein C, Morris R, Waterhouse L, Rapin I: Predictors and correlates of adaptive functioning in children with developmental disorders. J Autism Dev Disord 2001; 31:219-230.

NR90 Monday, May 22, 9:00 AM - 10:30 AM

Culture and Sick-Role Attitudes on Perception of Illness Severity and Disablility

MaryAnn Leynes, M.D. *Naval Medical Center San Diego, Mental Health, 2620 A Street, San Diego, CA, 92102*, James Spira, Ph.D., Robert McLay, M.D.

Educational Objectives:

Specific Objectives:

1. Is there a difference in beliefs of disability to quality of life across race?
2. Does the type of illness (mental vs. physical) predict beliefs of disability to quality of life?
3. Does the age of emigration predict beliefs of disability to quality of life in Filipinos?

Summary:

BACKGROUND: Many factors influence how patients perceive disability. Though not always recognized, the role of culture and ethnicity has long been an important element in the diagnosis and treatment of mental health. Although we serve a diverse patient population and recognize from our scope of practice that culture and ethnicity influence not only the patient's views on himself/herself but also what we may be able to offer as mental health providers, there is little formal studies done in this country to examine this phenomenon. We are interested in how cultural background influences attitudes toward the "sick-role" which in turn predict what differences may exist in perceived disability, quality of life, and prognosis of chronic and acute mental and physical illness.

METHODS: Patients in an outpatient psychiatric clinic were asked to read four vignettes describing health care cases and rate the degree to which the described individual was disabled and might be expected to recover. Via anonymous surveys, respondents were also asked information about their age, ethnicity, gender and view of their own mental and physical health. T-tests were used to compare disability scores and self-ratings of health given by males versus females and whites versus non-whites. Correlations were examined among disability scores, age and self-views of health.

RESULTS: Non-whites were found to rate individuals in the vignettes with slightly higher disability scores than were given by non-whites ($p<0.05$). No such differences were found in how patients of different ethnicities rated their own health. No effect of age or gender was found.

DISCUSSION: Perception of disability may provide valuable information not only for the patient but for the clinician in approaching treatment strategies for each individual. Continued study of more specific ethnicities and their perceptions would be warranted.

References:

1. Twaddle AC: Sickness Behavior and the Sick Role G K Hall & Co, 1979.
2. Lin M, inui TS, Kleinman AM, Womack WM: Sociocultural Dterminants of Help-seeking Behavior of Patients with Mental Illness. Journal of Nervous and Mental Disease 1982; 170:78-85.

NR91 Monday, May 22, 9:00 AM - 10:30 AM

Investigating the Relationship between Psychopharmacological Treatments and Change in Body Mass Index in a Clinical Sample of Child and Adolescent Patients With Psychiatric Diagnosises

Robert J. Love, D.O. *University of Texas at San Antonio, Department of Psychiatry, Floyd Curl Dr., San Antonio, TX, 78254*, Ashley S. Love, D.P.H., Rachel Ballard, M.D., Thomas L. Matthews, M.D., Michelle S. Guchereau, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the lack of statistically significant association between exposure to various classes of psychopharmacological agents and weight gain in terms of Body Mass Index (BMI) as well as BMI Z-score that were observed in a sample of child and adolescent psychiatric patients treated in an outpatient clinic setting. The participant should also be able to recognize that neither the number of medications used, nor the presence or absence of previous exposure to psychiatric medications, had an observed differential impact on weight gained in this group.

Summary:

Objective: To determine if any associations would be observed between change in BMI/BMI Z-score, psychotropic medication administration, and several potentially confounding variables in clinical sample of child and adolescent psychiatric outpatients.

Method: Retrospective analyses of 250 charts of patients who received treatment in an outpatient clinic during 18 month period prior to these analyses were performed. Of these charts, 204 contained adequate follow-up information. Multiple comparisons were performed using repeated measures analyses of covariance.

Result: There was significant change in BMI ($p=.05$), but not a statistically significant change in BMI-Z-score, on all the children from baseline to follow-up. The mean and median number of days on stable regimen was 721.7 and 460.5 respectively. There were no statistically significant effects on the change in BMI/BMI Z-score that were revealed when comparison was performed with: age; gender; class of psychotropic medication used (including: atypical antipsychotic, antidepressant, mood stabilizer, and stimulant medications); total number of medications; total time of exposure; or exposure to psychotropic medication prior to observation period.

Conclusions: After comparing the changes in BMI/BMI Z-score between patients differentiated by various stated parameters, we did not find any statistically significant associations between any of these factors and change in BMI/BMI Z-score.

References:

1. Vieweg, WVR, Kuhnley, LJ, Kuhnley, EJ, Anum, EA, Sood, B, Pandurangi, A, and Silverman, JJ. Body mass index (BMI) in newly admitted child and adolescent psychiatric inpatients.

Progress in Neuropsychopharmacology & Biological Psychiatry 2005; 29:51.

2. Ratzoni G, Gothelf D, Brand-Gothelf A, Reidman J, Kikinzon L, Gal G, Phillip M, Apter A, Weizman R. Weight Gain Associated With Olanzapine and Risperidone in Adolescent Patients: A Comparative Prospective Study. J. Am. Acad. Child Adolesc Psychiatr.

NR92 Monday, May 22, 9:00 AM - 10:30 AM

Risk Factors and Impact of Psychosis on Dementia of Alzheimer's Disease

Nahla A. Mahgoub, M.D. *Bergen Regional Medical Center, Psychiatry, 501 Eastbrook Road, Ridgewood, NJ, 07450-2112,* Asghar Hossain, M.D.

Educational Objectives:

Objective:

At the conclusion of the presentation the participants will recognize the risk factors associated with psychosis in dementia of Alzheimer's disease and its impact on the course of illness.

Psychosis may appear during course of illness of dementia of Alzheimer's disease and risk factors vary. Studies showed that psychosis directly proportionates with functional and cognitive abilities.

A retrospective chart review of 66 patients in the geriatric unit at Bergen Regional Medical Center who were admitted during 2004 with diagnosis of dementia of Alzheimer's disease.

The data collected: age, gender, ethnicity, age of onset, duration of illness, psychotic features, score of mini-mental status examination, global assessment of function, family history.

By reviewing the data, higher incidence of psychosis was found in Caucasian females with duration of illness 1-3 years and age of onset 78 -83 years. Alzheimer demented patients with psychosis had lower scores on mini-mental status examination and global assessment of function.

Summary:

Objective:

To assess the risk factors associated with psychosis in dementia of Alzheimer's disease and its impact on the course of illness.

Background:

Psychosis may appear during course of illness of dementia of Alzheimer's disease and risk factors vary according to different studies. Some studies have shown that the psychotic symptoms directly proportionate with the functional and cognitive abilities.

Method:

A retrospective chart review of 66 patients in the geriatric unit at Bergen Regional Medical Center who were admitted between January 2004 and December 2004 with diagnosis of dementia of Alzheimer's disease.

The data collected included age, gender, ethnicity, age of onset, duration of illness, psychotic features, score of mini-mental status examination, global assessment of function, family history of dementia of Alzheimer's disease and psychiatric illness.

66 % of patients with diagnosis of dementia of Alzheimer's disease presented with psychosis. Of these patients, 99 % had delusion, 55 % were Caucasian females, and 36 % had family history of psychiatric illness.

Of total admission, 38 % of Alzheimer demented patients with psychosis had mini-mental status examination score between 13-18 comparing to 6 % of Alzheimer demented patients without psychosis who had score in the same range. 36 % of Alzheimer demented patients with psychosis had global assessment of function between 19-24 comparing to 15 % of Alzheimer demented patients without psychosis who had score in the same range.

Conclusion:

Higher incidence of psychotic symptoms was found in Caucasian females with duration of illness between 1-3 years and age of onset between 78 -83 years. Delusion appeared more frequent than hallucination. Alzheimer demented patients with psychosis showed to have lower scores on mini-mental status examination and lower global assessment of function

References:

1. Journal Article - Paulsen JS, Salmon DP, Thal LJ: Incidence of and risk factors for hallucinations and delusions in patients with probable AD. Neurology 2000 Oct 24; 55(8): 1240-1.

2. Journal Article - Alberca R, Gil-Neciga E, Salas D: Psychotic symptoms and Alzheimer's disease. Neurologia 2000 Jan; 15(1): 8-14.

NR93 Monday, May 22, 9:00 AM - 10:30 AM

Dorsolateral Prefrontal-Anterior Cingulate Ccortices Activation in Children With Depressive Symptoms During the External Induction of Sadness

Adham Mancini-Marïe, M.D. *Centre de recherche de l'Hôpital Sainte-Justine, Department of Developmental Research and Prevention of Psychopathology, 7331 Rue Hochelaga, Montreal, PQ, H1N 3V2, Canada,* Mario Beauregard, Ph.D., Boualem Mensour, Ph.D., Gilles Beaudoin, Ph.D., Michel Boivin, Ph.D., Daniel Pérusse, Ph.D.

Educational Objectives:

At the conclusion of this presentation, we show that functional magnetic resonance imaging could be a potential technique is diagnosing early depression symptoms occurring during childhood, and therefore allowing for early intervention.

Summary:

Abstract

Objective: We sought to compare brain activation patterns in healthy and depressed children during the external induction of sadness using functional MRI (fMRI).

Method: Fifteen normal (N) controls and ten children with depressive symptoms (DS) were scanned with fMRI during the passive viewing of sad and emotionally neutral stimuli.

Results: Both groups activated the anterior cingulate cortex (ACC), but DS children exhibited less right dorsolateral prefrontal cortex (DLPFC) activation during sad stimuli relative to normal subjects.

Conclusion: Normal children activated the ACC and DLPFC and thus were able to process and regulate sadness. However, DS children activated the ACC only, thereby processing sad stimuli without the normal involvement of emotion regulation. These results suggest that depressive symptoms in childhood may be primarily related to a disturbance of the DLPFC-mediated down-regulation of sadness- which in turn may lead to the persistent and recurrent negative affect generally observed in depression.

References:

1. Drevets WC, Price JL, Simpson JR, Jr., Todd RD, Reich T, Vannier M, Raichle ME: Subgenual prefrontal cortex abnormalities in mood disorders. Nature 1997; 386(6627):824-7.

2. Mayberg HS, Brannan SK, Mahurin RK, Jerabek PA, Brickman JS, Tekell JL, Silva JA, McGinnis S, Glass TG, Martin CC, Fox PT: Cingulate function in depression: a potential predictor of treatment response. Neuroreport 1997; 8(4):1057-61.

NR94 Monday, May 22, 9:00 AM - 10:30 AM

Characteristic of Pathological Gamblers Based on Preferred Gambling Style: Strategic Versus Non-Strategic

Patrick J. Marsh, M.D. *University of South Florida, Psychiatry and Behavioral Health, 310 Paris Streeet #E, Tampa, FL, 33604,* Jon E. Grant, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to;

1. recognize the different styles of gambling amoung Pathological Gamblers
2. understand the clinical characteristics associated with gambling styles
3. recognize the importance of screening for comorbid conditions based on gambling style

Summary:

Abstract

Background: Although prior studies have examined various clinical correlates of pathological gambling, no study to date has analysed how the clinical features of pathological gambling relate to gambling style.

Method: 190 consecutive subjects with DSM-IV pathological gambling (55.3% females; mean age = 51.5 ± 7.4) were grouped by primary gambling style - strategic (e.g. cards, dice, sports betting, stock market) (n=77; 40.5%) versus non-strategic (e.g. slots, video poker, pull tabs) (n=113; 59.5%). We compared the groups on the following variables: clinical characteristics, gambling severity (using the Yale-Brown Obsessive-Compulsive Scale Modified for Pathological Gambling), psychiatric comorbidity (using the Structured Clinical Interview for DSM-IV), and social and occupational functioning.

Results: Non-strategic gambling style was significantly associated with females (72% compared to 34%) ($p<.001$). Mood disorders and alcohol use disorders were the most common co-morbidities in both groups with no significant difference between groups. Subjects who preferred non-strategic forms of gambling reported higher lifetime rates of substance use disorders involving drugs of stimulation (cocaine, amphethamine, and nicotine) ($p<.001$), and significantly more hours spent gambling each week (18 hrs compared to 11hrs) ($p<.01$). Gambling severity or functioning did not differ significantly between groups.

Conclusion: These preliminary results suggest that gaming choices may be associated with specific comorbid disorders. Clinicians may want to screen for certain comorbidities based on client's chosen gaming style.

References:

1. Petry NM: A comparison of treatment-seeking pthological gamblers based on preferred gambling activity. Addiction 2003; 98:645-655.
2. Grant JE, Kim SW: Demographic and Clinical Characteristics of 131 Pathologic Gamblers. J Clin Psychiatry 2001; 62: 957-961.

NR95 Monday, May 22, 9:00 AM - 10:30 AM

The Functional Outcome of Patients With Euthymic Bipolar Disorder: Impact of Clinical, Cognitive, and Pharmacological Factors

Anabel Martinez-Aran *Hospital Clinic, Villarroel 170, Barcelona, 08036, Spain,* Carla Torrent, Claire Daban, Jose Sanchez-Moreno, Rafael Tabares-Seisdedos, Jose Luis Ayuso-Mateos, Eduard Vieta

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize those factors that may be influence the psychosocial functioning of bipolar patients.

Summary:

Introduction: Few studies have examined the clinical, neuropsychological, and pharmacological factors involved in the functional outcome of bipolar disorder despite the gap between clinical and functional recovery.

Methods: A sample of 77 euthymic bipolar patients were included in the study. Using an a priori definition of poor versus good functional outcome, based on the psychosocial items of the General Assessment of Functioning (GAF, DSM-IV), and taking also into account their occupational adaptation, the patients were divided into two groups; good or poor occupational functioning. Highly (n=46) and poorly (n=31) functioning patients were compared on several clinical, neuropsychological and pharmacological variables and the two patient groups were contrasted with healthy controls (n=35) on cognitive performance.

Results: Highly and poorly functioning groups did not differ with respect to clinical variables. However, bipolar patients in general showed poorer cognitive performance than healthy controls. This was most evident in poorly functioning patients and in particular on verbal memory and executive function measures.

Conclusions: Poorly functioning patients were cognitively more impaired than highly functioning patients on verbal recall and executive functions. The variable that best predicted psychosocial functioning in bipolar patients was verbal memory.

References:

1. Martinez-Aran A, Vieta E, Reinares M, Colom F, Torrent C, Sanchez-Moreno J, Benabarre A, Goikolea JM, Comes M, Salamero M: Cognitive function across manic or hypomanic, depressed, and euthymic states in bipolar disorder. Am.J Psychiatry 2004; 161:262.
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NR96 Monday, May 22, 9:00 AM - 10:30 AM

The Relation Between Coping and Quality of Life in Schizophrenia: Re-analysis

Jennifer N. Martins *University of Western Ontario, Honours B.Sc Psychology, 310 Central Ave rear lower, London, ON, N6B2C8, Canada*, Abraham Rudnick, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to: analyze the structure of coping factors in schizophrenia and analyze the relation between coping strategies and quality of life in patients with schizophrenia

Summary:

Background and objectives: Problem-focused versus emotion-focused coping is considered to have beneficial effects on outcome in stressful situations, including in severe and persistent illnesses. This has not been strongly corroborated for schizophrenia. Lysaker et al recently generated and studied a framework of coping in schizophrenia, which was found to partly predict vocational function. We re-analyzed data from a previous study using Lysaker et al's coping factors to test their relation to quality of life (QoL) and to symptom severity in schizophrenia. Method: 58 adult outpatients, diagnosed with schizophrenia as per SCID, tested at one point in time on the Positive and Negative Symptom Scale (PANSS), the Ways of Coping Checklist (WCC), and the Wiscon-

sin Quality of Life Index (W-QLI). Data analysis was performed by forcing Lysaker et al's coping factors on the WCC scores, and correlating these coping factors with the W-QLI and the PANSS scores. Results: All of Lysaker et al's coping factors were (negatively) correlated with the quality of life domain of finances. The coping strategies of considering, acting, positive appraisal, and self-soothing were (negatively) correlated with negative symptom severity. Principal components factor analysis did not demonstrate a coherent factor structure of the coping strategies. Conclusion: Few significant correlations were found. Further research should be conducted on existing and novel frameworks of coping, in order to establish effective coping in schizophrenia.

References:

1. Rudnick A: The impact of coping on the relation between symptoms and quality of life in schizophrenia. Psychiatry 2001; 64(4): 304-308.
2. Lysaker PH., Johannesen J., Lancaster RS., Davis LW, Zito W., & Bell MD: Assessing coping in schizophrenia ' a rationally devised scoring scheme to assess coping in schizophrenia. International Journal of Psychosocial Rehabilitation; 8: 73-83.

NR97 Monday, May 22, 9:00 AM - 10:30 AM

Dementia and Suicide: The Role of Narcissism

Daniel Matusevich, M.D. *Hospital Italiano, Psychiatric Unit, Buenos Aires, 1004, Argentina*, Martin Ruiz, Carolina Vairo, Carlos A. Finkelsztein, Alfredo Job, Mariana Pedace, Gustavo Rozadilla

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the important role of narcissism as a risk factor for suicide attempt in dementia patients.

Summary:

Objective: To determine, in older inpatients with dementia, differences between narcissistic personality disorder and no personality disorder as regards the following causes of admission: suicide attempt, behavioral and psychological symptoms of dementia, psychotic episode, diagnostic assessment, substance abuse, depression and suicide ideas.

Material and methods: This is a comparative, prospective, observational, transversal single blind study.

Results: We studied 67 inpatients with dementia. Statistical significant associations were found between narcissistic personality disorder and suicide attempt ($p=0.022;\chi^2=5.21;CL=0.88-37.75$) and narcissistic personality disorder and suicide ideas ($p=0.023;\chi^2=5.16;CL=0.95-17.52$). Also we found significant associations between living alone and narcissistic personality disorder with dementia ($p=0.005;\chi^2=7.69;CL=1.30-17.83$).Discussion: Although associations between narcissistic personality disorder and suicide ideas and attempts in patients with dementia have not been reported, there seems to be a relation between them, in patients with early dementia with perception of their deterioration were narcissism and hate of ageing plays a crucial role. This should be taken into account to prevent suicide in older age not always related to depression.

References:

1. Uncapher H, Gallagher TD, Osgood N, Bongar B. Hopelessness and suicidal ideation in older adults. Gerontologist 1998; 38: 62-70.
2. Draper B, Mac Cuspie-Moore C, Brodaty H. Suicidal ideation and the "wish to die" in dementia patients: the role of depression. Age Aging 1998; 17: 503-507.

NR98 Monday, May 22, 9:00 AM - 10:30 AM

Defenses Predict Basic and Social Emotions During Stress in Adolescents

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Educational Objectives:

1. To educate the practitioner regarding the role of defenses in normative development in adolescents
2. To highlight differences in emotion regulation as a function of defenses

Summary:

Objective: To demonstrate the role of defenses in adolescents during moderately stressful tasks. The modern concept of defenses views them as habitual meaning attribution systems. We postulated that 1. Immature defenses would predict activation of negative basic (anger, fear, sadness) and social (guilt; shame) emotions across time and tasks; 2. Mature defenses would predict the activation of positive basic (happiness, interest, pleasure) emotions across time and tasks.

Methods: We studied 163 high school students (54% female, mean age 16; SD=1; ethnically diverse). Subjects completed the Response Evaluation Measure (REM-71), the Weinberger Adjustment Inventory (WAI, well established instruments for the measurement of defenses and personality.; and completed the Stress Inducing Speech Task (SIST) which measures anticipated (B/L), defined (STR) and unstructured stress (FA).

Results: Our hypotheses were confirmed. Immature defenses predicted activation of negative basic and background, and social emotions. Mature defenses predicted activation of positive emotions (Pearson's r between .16 and .39; all p's<0.05). Activation patterns were maintained, regardless of the task.

Conclusion: This is the first study to report specific emotion activation profiles on a habitual basis and across tasks of differing character. The results have implications for normative development, stress reactivity, trauma related psychopathology and psychotherapy.

References:

1. Journal article - Steiner H, Ryst E, Berkowitz J, Geschwendt M, Carrion V, Koopman C: Boys' And Girls' Responses to Stress: Affect and Heart Rate During a Speech Task. J Adolescent Health, 2002, 30S:14-21.
2. Journal Article - Steiner H,Araujo L, Koopman C. The Response Evaluation Measure: A New Instrument For The Assessment Of Defenses. Am J Psychiatry 2001, 158 (3): 467-473.

NR99 Monday, May 22, 9:00 AM - 10:30 AM

Meta-Analysis of Risperidone as a Treatment for Tourettes Disorder

Karl Meisel, M.A. *Michigan State University, College of Human Medicine, 317 1/2 E. Crescent, Marquette, MI, 49855*

Educational Objectives:

At the conclusion of the presentation, the audience should understand the level of evidence supporting risperidone as a therapeutic option to treat Tourette disorder (TD). The audience will learn about common side effects often associated with standard therapies, which commonly cause discontinuation. They will understand the mechanism of action of risperidone and the rational for its use. In addition, the strength of the evidence for risperidone use will be discussed, and why it is advantageous to use a meta-analysis to increase the statistical power of previous studies. The participants should learn the results of this study, which showed

that risperidone is equivalent to other standard therapies like primozide and clonidine (-.15 mean difference [95% CI -.56, .26]). The forest-plot analysis demonstrates that no statistical significance exists between the effect size of risperidone and other active controls. However, risperidone has the added benefit of treating co-morbid OCD in Tourettes patients, which occurs in 40% of TD. Therefore, risperidone may be more advantageous as a therapy for TD compared to other standard treatments.

Summary:

Introduction: Dopamine receptor antagonists are the current standard therapy for Tourette disorder (TD). However, severe extrapyramidal side-effects limits the use of these agents. Risperidone, a benzisoxazole derivative, offers the potential advantages of equivalent efficacy and reduced side-effects because it blocks 5HT 5-HT2A receptors, and D2 dopamine receptor. Objective: This study investigated whether risperidone is an equivalent treatment for TD compared to pimozide and clonidine. Also, the side effect profile of standard therapy and risperidone was compared. Method: The author used meta-analytic methods to increase the statistical power of small RCTs. Only randomized controlled trials that compared risperidone to an active control for the reduction of tics in TD patients were considered for this analysis. A search of Medline, Ovid, dissertations, and the Cochrane databases yielded three active controlled trials, which were included in this meta-analysis. Results: This meta-analysis demonstrates that risperidone is equivalent to standard therapy for TD (-.15 mean difference [95% CI -.56, .26]). The forest-plot analysis demonstrates that no statistical significance exists between the effect size of risperidone and other active controls. However, risperidone has the added benefit of treating the 40% of TD patients with co-morbid OCD. There appears to be fewer side effects associated with risperidone treatment compared to either pimozide or clonidine, which is not in agreement with previous literature. Therefore, risperidone may be more advantageous as a therapy for TD compared to other standard treatments. Conclusion: Further trials are needed to explore the efficacy of risperidone in chronic use and its associated side-effects in TD patients. Current studies that are available only enrolled a total of 109 patients, thus limiting the effect size that is detectable. Also, future studies should include objective measures of side effects associated with treatment in order to better understand relative benefits of competing treatment options.

References:

1. Bruggeman R, Linden C, et. al: Risperidone Versus Pimozide in Touretteâ™s Disorder: A comparative Double-Blind Parallel-Group Study. J Clin Psychology 2001;62(1): 50-56.

2. Gaffney G, Perry P, et al: Risperidone Versus Clonidine in the Treatment of Children and Adolescents With Touretteâ™s Syndrome. J Am Acad Child Adolesc Psychiatry 2002;41(3): 330-336.

NR100 Monday, May 22, 9:00 AM - 10:30 AM

Association Study of ADHD and the Gene for Dopamine Recepter D2: *DRD2*

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand the latest findings relating to the DRD2 gene as a candidate for involvement in genetic susceptibility to ADHD, and to recognize how the implications of these findings may provide direction for future work.

Summary:

Objective: The DRD2 gene has been tested for involvement in ADHD by several investigators, with largely negative results. However, these have been based almost exclusively on analyses of one single nucleotide polymorphism (SNP), *Taq*IA, located outside the gene. Thus, it would be premature to exclude DRD2 from consideration on this basis alone. Our objective was to test for association between DRD2 and ADHD using a more extensive approach involving five polymorphisms spanning the gene.

Methods: The polymorphisms analysed include the *Taq*IA SNP and the following additional markers: -141C*Ins/Del*, a promoter region insertion/deletion polymorphism; *Taq*IB, a SNP in intron 1; $(CA)_n$STRP, a microsatellite in intron 2; and Ser311Cys, a coding SNP in exon 7. To test for association with ADHD, we used the transmission/disequilibrium test (TDT), a family-based method that tests for biased transmission of alleles or haplotypes (allele combinations) from heterozygous parents to their affected children. Given evidence that working memory impairment may be prevalent in ADHD, and that D2 receptors may contribute to working memory function, we also performed quantitative analyses investigating the inheritance of these polymorphisms in relation to performance on a verbal working memory task (Digit Span Backwards).

Results: TDT analysis of 169 families (with 211 affected children) did not show evidence for biased transmission of any of the single alleles or haplotypes ($p>0.05$). We note, however, that for the Ser311Cys polymorphism there were too few informative transmissions to provide a definitive result. The quantitative analyses also showed no evidence for association of the DRD2 gene with working memory function in our study sample.

Conclusions: Although definitive conclusions regarding the Ser311Cys polymorphism will await collection of a larger study sample, our findings do not support involvement of DRD2 in ADHD.

Funding source: CIHR

References:

1. Faraone SV, Perlis RH, Doyle AE, Smoller JW, Goralnick JJ, Holmgren MA, Sklar P: Molecular genetics of attention-deficit/hyperactivity disorder. Biol Psychiatry 2005; 57:1313-23.

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NR101 Monday, May 22, 9:00 AM - 10:30 AM

Obsessive Compulsive Characteristics Persist After Recovery From Bulimia Nervosa

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Educational Objectives:

At the conclusion of the session, the participant should be able to characterize the extent to which obsessive-compulsive symptoms are observed in individuals with current or past episodes of bulimia nervosa.

Summary:

Although the primary symptoms of bulimia nervosa (BN) involve abnormal eating patterns, some studies have indicated co-morbid obsessive and compulsive (OC) behaviors. This study compared OC characteristics in individuals with BN and healthy controls using subject self-ratings on the Maudsley Obsessive-Compulsive

Inventory (MOCI), and evaluated whether elevated MOCI scores persist in individuals who have recovered from BN (RBN).

MOCI scores were available for medication-free, normal weight women with BN (n=25), RBN (n=21) and healthy controls (n=28) who participated in previous studies of neurotransmitter function. Subjects also completed the Eating Attitudes Test (EAT) and Spielberger Trait Anxiety Inventory (STAI). Ratings for the patient groups were compared to controls by Dunnett t-test and Mann-Whitney Test.

MOCI scores for the BN group were, as expected, significantly elevated in comparison to controls (5.4 ± 4.4 versus 2.5 ± 1.9; $p<0.02$). Of note, MOCI scores for the RBN group (5.5 ± 5.4) were similar to values for the BN subjects and were also elevated in comparison to controls ($p<0.05$). In contrast, scores on the EAT and STAI for the RBN subjects were significantly reduced in comparison to BN ($p<.01$), although still significantly higher than for controls ($p<.01$).

These findings extend previous reports indicating that the OC symptoms present in subjects with BN persist following remission, suggesting that elevated OC ratings may reflect a stable trait characteristic of individuals who develop BN.

Supported in part by USPHS grant R01 MH45466.

References:

1. Wolfe BE, Metzger ED, Levine JM, Finkelstein DM, Cooper TB, Jimerson DC. Serotonin function following remission from bulimia nervosa. Neuropsychopharmacology 2000;22:257-263.

2. Kaye WH, Greeno, CG; Moss, H; et al. Alterations in serotonin activity and psychiatric symptoms after recovery from bulimia nervosa. Arch Gen Psych 1998;55:927-935.

NR102 Monday, May 22, 9:00 AM - 10:30 AM

Atypical Antipsychotics and Metabolic Screening: Four-State Medicaid Study

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Educational Objectives:

At the conclusion of this presentation, the participant should recognize the prevalence of glucose and lipid monitoring associated with the usage of atypical antipsychotic medications.

Summary:

Some atypical antipsychotic (AA) drugs have associated risk of hyperglycemia and dyslipidemia, with recent recommendations that all treated patients undergo blood glucose and lipid monitoring. The prevalence of monitoring associated with AA prescription is understudied. This retrospective cohort study used Medicaid claims data from California, Oregon, Tennessee, and Utah to evaluate 55,308 patients who received an antipsychotic drug between 1998 and 2003. Laboratory testing was identified with CPT-4 codes. Multivariate logistic regression determined likelihood of baseline glucose testing (BGT) adjusting for drug, year, and clinical characteristics. Initiation of AA treatment was associated with a 5% increase in glucose testing ($p<0.001$) and 2% increase in lipid testing ($p<0.001$) over background test levels. Combining AA-related increases plus background rate, the overall prevalence of baseline testing (-14 days/+28 days) was 18% (glucose) and 6% (lipid). Compared to risperidone, BGT was higher with olanzapine (OR=1.14, 95% CI: 1.08-1.21) and lower with ziprasidone (OR= 0.68, 95% CI: 0.54-0.86). BGT was higher in 2003 versus 1998 (OR=2.78, 95% CI: 2.44-3.13). Metabolic screening prevalence remained low over the time period of observation. Research is needed to evaluate monitoring prevalence following recent recommendations.

References:

1. ADA, APA, AACE, NAASO: Consensus development conference on antipsychotic drugs and obesity and diabetes. J Clin Psychiatry. 2004; 65:267-272.

2. Newcomer JW, Nasrallah HA, Loebel AD: The atypical antipsychotic therapy and metabolic issues national survey. J Clin Psychopharmacol. 2004; 24: S1-S6.

NR103 Monday, May 22, 9:00 AM - 10:30 AM

Adjunctive Zonisamide for Treatment Refractory Anxiety Disorders

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize and understand the potential clinical use of adjunctive zonisamide in the treatment of anxiety.

Summary:

Objective: To assess the use of a novel anticonvulsant, zonisamide, in patients with treatment refractory anxiety.

Method: Pilot and open study of a cohort of patients with anxiety (n=10), who were deemed partial or non-responders to anxiolytic therapy, and received adjunctive zonisamide in a naturalistic fashion. The primary outcome measures were the Hamilton Anxiety Scale (HAM-A), the Clinical Global Impression of Severity (CGI-S) and the Clinical Global Impression of Improvement (CGI-I).

Results: Patients included were markedly ill with a mean number of previous medication trials of 4.9 ± 1.9, a baseline HAM-A score of 27.9 ± 3.8, and a baseline CGI-S score of 5.7 ± 0.5. Patients improved significantly with an endpoint HAM-A score of 12.6 ± 7.4 ($p<0.001$), CGI-S score of 3.6 ± 1.3 ($p<0.002$), and CGI-I score of 2.5 ± 1.3. Zonisamide at a mean ± SD dose of 160 ± 70 mg/day for 9.2 ± 4.5 weeks was generally well tolerated. Adverse events were generally mild, and included sedation, tiredness, agitation, and dizziness. No patients discontinued zonisamide due to side effects. Six patients (60%) met responder criteria at end point (CGI-I ≤ 2).

Conclusion: Results from this pilot and open naturalistic study suggest that zonisamide may effectively augment response to anxiolytic medications in patients with treatment refractory anxiety. Larger and controlled studies are warranted to confirm these preliminary findings.

References:

1. Okada M, Hirano T, Kawata Y, Murakami T, Wada K, Mizuno K, Kondo T, Kaneko S. (1999) Biphasic effects of zonisamide on serotoninergic system in rat hippocampus. Epilepsy Res;34:187-197.

2. Kinrys G and Wygant L: Anticonvulsants in anxiety disorders. Current Psychiatry Rep. 2005 Aug:7(4):258-67.

NR104 Monday, May 22, 9:00 AM - 10:30 AM

The Difference of a Diet: Retrospective Study Assessing Weight and BMI Changes Among Hospitalized Patients Taking Olanzapine Before and After Implementation of Behavioral Modifications

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David Franklin, Psy.D., Hilary Parker, B.A., Gerald A. Maguire, M.D., Lawrence Plon, Pharm.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that diet modifications are an effective means of reducing weight gain among hospitalized patients with schizophrenia or schizoaffective disorder treated with olanzapine.

Summary:

Background: Olanzapine is a highly effective atypical antipsychotic that can induce significant weight gain. Although behavioral modification programs have been shown to decrease weight among outpatients, few studies have focused on changing the inpatient diet. In January, 2003, the Acute Psychiatric Unit of UCI Medical Center introduced a new diet program that eliminated second servings, desserts, sodas and high caloric snacks. This retrospective study compares the weight and BMI changes of patients treated with olanzapine before and after the new diet was implemented.

Methods: An electronic review of patients at the Acute Psychiatric Unit of UCI Medical Center from January 1998 to December 2004 was performed. Patients with schizophrenia or schizoaffective disorder who received olanzapine for 1-7 weeks were selected.

Results: Patients on a standard diet, N=48, gained an average of 9.4 pounds, compared to patients on a modified diet, N=95, who gained 3.7 pounds (P=0.0015). Increase in BMI was greater for the standard diet group versus the modified diet group (P= .003). Average treatment time with olanzapine was 20.2 days in the modified diet group versus 22.7 days in the standard diet group (P=.188).

Conclusions: Diet modifications are a simple and efficacious means of reducing weight gain among patients with schizophrenia or schizoaffective disorder treated with olanzapine in an inpatient setting.

References:

1. Journal Article: Allison DB, Casey DE. Antipsychotic-induced weight gain: a review of the literature. Journal of Clinical Psychiatry 2001; 62:S22-S31.
2. Journal Article: Wirshing DA, Wirshing WC, Kysar L et al. Novel antipsychotics: comparison of weight gain liabilities. Journal of Clinical Psychiatry 1999; 60-358-363.

NR105 Monday, May 22, 9:00 AM - 10:30 AM

Maintenance CBT in Preventing Relapse in Patients on SSRI Continuation

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Educational Objectives:

To understand the utility of maintenance CBT in preventing relapse in patients who are on prophylactic SSRI treatment to prevent relapse

Summary:

The utility of cognitive-behavioral therapy in the treatment of acute depression has been well established. It is frequently employed with antidepressants acutely to yield greatest efficacy. While it is frequently stated that the techniques of Cognitive-Behavior Therapy learned during acute treatment are enduring there is little data suggesting this is true

We studied 327 patients over a 13 year period in a community clinic who responded to one of four SSRIs (SSRI's) with a 50% reduction in Montgomery Asberg Score after 12 weeks treatment. SSRI's used were fluoxetine, citalopram, paroxetine and sertraline. A Dysfunctional Attitude Scale (DAS) was given to all patients after this period. The patients were all followed on the medication to which they responded until they either relapsed, dropped out, or terminated well (were well as of Nov 1, 2005 the endpoint of the study)

Overall 110 patients acutely received Cognitive-Behavior Therapy in addition to the SSRI and 217 did not. Patients who received Cognitive-Behavior Therapy acutely had at the end of the acute trial significantly lower MADRS (5.36 versus 7.89 p<.0001) and DAS scores (69.28 versus 81.54 p<.0001) than the group that not receiving Cognitive-Behavior Therapy

Following acute response 35 of the 110 patients who received Cognitive-Behavior Therapy acutely elected to continue Cognitive-Behavior Therapy additve to the medication and 75 did not. Overall the group that continued Cognitive-Behavior Therapy remained well for 49.60 months as opposed to 34.77 months for those who did not continue Cognitive-Behavior Therapy . This difference was statistically significant (p<.015). Interestingly the 75 patients who received Cognitive-Behavior Therapy acutely but not for maintenance did not remain well longer than the 217 patinets who did not receive Cognitive-Behavior Therapy acutely (34.77 versus 30.78 p>.025)

In conclusion, Cognitive-Behavior Therapy additve to medication during acute treatment was not enduring long-term. However maintenance Cognitive-Behavior Therapy additive to SSRI's was effective in preventing relapse

References:

1. Peselow E, Robins C, Block P, et al: Dysfunctional Attitudes in Depressed Patients Before and After Clinical Treatment and in Normal Controls. Am J Psychiatry 1990;147:439-444.
2. Simons AD, Murphy G, Levine JJ, et al: Cognitive therapy and pharmacotherapy for depression; sustained improvement over 1 year. Arch Gen Psychiatry 1986;43:43-48.

NR106 Monday, May 22, 9:00 AM - 10:30 AM

Insomnia, Sleeping Pills, and Increased Mortality Risk

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Educational Objectives:

At the conclusion of this session, the participant should be alerted to the controversy over a possible relationship between insomnia, hypnotic use and increased mortality.

Summary:

Introduction: Insomnia and sleeping pills use, both of which have a high prevalence worldwide, are arguably associated with higher mortality risk.

Method: A review was done of the English language literature on insomnia, sleeping pill use and mortality.

Results: Kripke (1979), examining The Cancer Prevention Study I data (CPS I), including more than one million subjects, found an increased mortality risk in men with insomnia. Four other studies (Pollak, 1990; Kojima, 2000; Manabe, 2000, Nilsson, 2001) also reported an association between insomnia and an increased mortality risk. Kripke (2002), in a replication of his 1979 study found no association between insomnia and decreased longevity. No relationship between insomnia and an increased mortality was found in ten other studies (Rumble, 1992; Brabbins, 1993; Foley, 1995; Hays, 1996; Althuis, 1998; Jensen, 1998; Newman, 2000; Rockwood, 2001; Mallon, 2002; Phillips, 2005).

A correlative relationship between sleeping pill use and increased mortality risk was shown in both Caner Prevention Studies (Kripke 1979; 2002). Kojima (2000) found an increased mortality risk only in females. No relationship between sleeping pills use

and decreased longevity was found in six other studies (Pollak, 1990; Rumble, 1992; Brabbins, 1993; Hays, 1996; Mallon, 2002; Phillips, 2005).

Discussion: Insomnia and sleeping pills use were not consistently associated with an increased mortality rate. Definition of insomnia was poor and inconsistent. In most of the studies it was not determined what "sleeping pills" participants were taking. The design of the studies, the sample sizes, the age of the subjects, and the follow up period were variable across the studies, which made comparisons difficult.

Conclusion: Well designed, prospective double blind, randomized, long-term clinical trials with an adequate number of subjects, and the use of the DSM-IV-TR definition of insomnia are needed to improve our understanding of relationship between insomnia, hypnotic use and decreased longevity.

References:

1. Phillips B, Mannino DM. Does insomnia kill? Sleep. 2005 Aug 1; 28(8):965-71.
2. Kripke DF, Garfinkel L, Wingard DL, Klauber MR, Marler MR. Mortality associated with sleep duration and insomnia. Arch Gen Psychiatry. 2002; 59:131-136.

NR107 Monday, May 22, 9:00 AM - 10:30 AM

HLA Class I Associations With Schizophrenia, Schizoaffective Disorder, and Biological Relatives

Sandra Odebrecht Vargas Nunes, M.D. *Universidade Estadual de Londrina, Psychaitry, Av Adhemar de Barros #625, Av Bandeirantes, 625, Londrina, 86050190, Brazil*, Eiko NagasaKa Itano, Ph.D., Maria Angélica Ehara Watanabre, Ph.D., Tiemi Matsuo, Psy.D., Sueli Donizetti Borelli, R.G.N.

Educational Objectives:

The aim of this study was to determine the association of HLA in patients with schizophrenia, schizoaffective disorder, and biological relatives

Correlation of human leukocyte antigens (HLA). in psychiatric disorders

Summary:

The aim of this study was to determine the association of HLA in patients with schizophrenia, schizoaffective disorder, and biological relatives, in a Brazilian population. The subjects studied were 50 Patients with Schizophrenia and schizoaffective patients, 48 healthy controls, 41 first-degree relatives without psychiatric disease, and 48 first-degree relatives with mood disorder. They were interviewed by structured diagnostic criteria categorized according DSM-IV, axis I, (SCID-IV). The mean duration of illness in schizophrenic and schizoaffective patients was 15.3 years ± 9.9 and the median age of onset was 22.4 years ± 7.4. The group differed in educational background and marital status. Patients presented lower educational achievement ($p=0.004$) than controls and relatives, and most of them were unmarried ($p<0.001$), differently from controls and relatives. In patients there were more significant differences regarding occupational impairment than controls and relatives ($p<0.001$). Patients and relatives had no significantly HLA-A, HLA-DRB1 association. Significant HLA-B class I association was found with HLA- B*15 in patients ($p= 0.003$), family with humor disorder and without mental disorder ($p=0.003$). HLA -B*15 frequency was significantly increased in a subgroup of patients with age at onset in the early 20s, lower educational achievement, occupational disability, chronically ill, more paranoid type These findings suggest the existence of some involvement of an immunogenetic mechanism in a subgroup of schizophrenic, schizoaffective patients and biological relatives.

References:

1. Nunes, S.O.V.,Borelli,S, Matsuo T, Watanabe, MA, Itano,El. The association of the HLA in patients with schizophrenia, schizoaffective disorder, and their biological relatives. Shizopherenia Research,2005;{s.l.}.76: (.2/3),:195-198.
2. Wright, P., Nimgaonkar, V., Donaldson, P., Murray, R., 2001. Schizophrenia and HLA: a review. Schizophr. Res. 47, 1-12.

NR108 Monday, May 22, 9:00 AM - 10:30 AM

Phosphorylation of DARPP-32 After Electroconvulsive Shock in Rat Striatum

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Educational Objectives:

DARPP-32 seems to be an important molecule for psychotic disorder and substance abuse because it is known to be a key mechanism for integration of signals via dopaminoceptive neurons and the relationship of dopamine, glutamate and DARPP-32 is suggested. Understanding of the change of phosphorylation pattern induced by ECS will elucidate the mechanism of psychosis and substance abuse.

Summary:

Electroconvulsive shock (ECS) is known to activate dopaminergic signaling in the striatum. DARPP-32 is abundant in the striatum and the phosphorylation of DARPP-32 is a key mechanism for integration of signals via dopaminoceptive neurons. The phosphorylation at Thr34 by protein kinase A(PKA) makes it an inhibitor of protein phosphatase-1, while the phosphorylation at Thr75 by Cdk5 makes it an inhibitor of PKA. We examined the phosphrylation of DARPP-32 to show the effect of ECS in rat striatum. Male Sprague-Dawley rats were treated with ECS and were decapitated at 0, 2, 10, 30 minutes, 1 and 3 hours after ECS. Immunoblotting was done to identify the expression of DARPP-32 and the phosphorylation at Thr 34 and Thr 75. Immunohistochemical staining was done to identify the distribution of DARPP-32 in the striatum. The phosphorylation of DARPP-32 at Thr 34 showed continous increase until 3 hours after ECS. The phosphorylation at Thr 75 reached the maximum 2 to 10 minutes after ECS. DARPP-32 showed preferential phosphorylation in the ventral striatum compared to the dorsal striatum. ECS has an effect on DARPP-32 phsphorylation pattern, to the direction of general increase in the protein phosphorylation.

References:

1. Svenningsson P:DARPP-32: An Integrator of Neurotransmission. Annu Rev Pharmacol Toxicol 2004;44:269-296.
2. Nishi A:Bidirectional regulation of DARPP-32 phosphorylation by dopamine. J Neurosci 1997;17:8147-8155.

NR109 Monday, May 22, 9:00 AM - 10:30 AM

Assessment of the Quality of Life in Hospice Patients With Cancer at the Very End of Life

Hayley Pessin, Ph.D. *Memorial Sloan-Kettering Cancer Center, Psychiatry, 1275 York Avenue, Department of Psychiatry, New York, NY, 10021*, Jennifer Abbey, M.A., Barry D. Rosenfeld, Ph.D., William Breitbart, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to better assess quality of life quality of life in severely ill cancer patients in palliative care hospice settings.

Summary:

Introduction: Quality of life has been targeted as an important outcome variable in the assessment of well-being at the end of life. Researchers have designed measures specifically targeting quality of life at the end of life, reducing emphasis on physical functioning and underscoring psychosocial concerns. However, the majority of the the measure validation studies were conducted in outpatients with advanced illness. Therefore, it is important to assess whether these measures of QOL remain salient for imminently dying hospice patients with cancer.

Methods: 86 patients in a palliative care hospital with a life expectancy of less than 1 month completed a psychosocial interview of standardized instruments. Quality of life was assessed using the QUAL-E (Steinhauser et al, 2002, 2004) and the McGill QOL Index. Correlational analyses were completed using the: HDRS, HADS, BHS, LOT, MSAS, BPI, and FACIT-SWB.

Results: The QUAL-E demonstrated good validity as a global measure of quality of life and correlated with the McGill QOL index. The 4 subscales demonstrated good convergent and discriminant validity. *Life completion* was associated with quality of life, hopelessness, optimism, spiritual well-being, and social support; *Symptom impact* was associated with physical symptoms and symptom distress, anxiety, depression, desire for death, and spiritual well-being; *Relationship with health care provider* was associated with quality of life, hopelessness, spiritual well-being, physical symptom distress, and pain; *Preparation for end of life* was associated with quality of life, hopelessness, optimism, physical symptoms and physical symptom distress, anxiety, depression, and desire for death

Conclusions: The QUAL-E is an appropriate and useful tool to aid in the challenging task evaluating quality of life at the end of life among hospice cancer patients. The QUAL-E is a brief measure targeting the concerns of severely impaired patients, and could be a valuable outcome measure for evaluating care at the end of life.

References:

1. Steinhauser KE, Bosworth HB, Clipp EC, Bosworth HB, McNeilly M, Christakis NA, Voils CI, Tulsky JA. Measuring quality of life at the end of life: Validation of the QUAL-E. J Palliat & Support Care 2004; 2(1): 3-14.
2. Steinhauser KE, Bosworth HB, Clipp EC, McNeilly M, Christakis NA, Parker J, Tulsky JA. Initial assessment of a new instrument to measure quality of life at the end of life. J Palliat Med 2002; 5(6):829-41.

NR110 Monday, May 22, 9:00 AM - 10:30 AM

Clinical Features Influencing Long-Term Lithium Treatment Outcome in Patients With Bipolar Disorder

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Educational Objectives:

At the conclusion of this session the participant should be able to assess clinical features of his bipolar patient to predict long-term prophylactic treatment efficacy of Lithium. The participant learned which statistical models are suited best to analyze long-term outcome data.

Summary:

Objective:

In many patients with bipolar disorders, lithium can prevent or reduce multiple recurrences and the disabling course of the illness. To assess the influence of atypical features on treatment outcome, the International Group for the Study of Lithium Treated Patients (IGSLI) investigated data from a large multicenter cohort treated up to 30 years.

Method:

We created complete data sets of 336 bipolar I and II patients containing clinical characteristics (e.g. demographics; typical and atypical features, such as psychiatric comorbidity, inter-episodes, and residual symptoms; and mood-incongruent psychotic features) and the course of treatment (e.g. recurrences including severity and comedication). To assess long-term outcome, we used both classical and extended Cox regression modeling, accounting for correlation due to multiple recurrences.

Results:

On the average, lithium treatment was initiated 10 years after the diagnosis of bipolar disorder, and during follow-up patients experienced approximately 5 episodes. The number of atypical features had a significant negative impact on long-term outcome, even after adjusting for factors such as the time elapsed between onset of illness and lithium treatment, the number of previous episodes, and comedication. Cox regression modeling looking only at time to first recurrence showed that the hazard for a new episode increased by approximately 40% with each additional atypical feature. Because the cumulative hazards of successive recurrences differed markedly, extended Cox models were better suited to evaluate the long-term outcome and revealed slightly smaller hazards. Frailty models that also accounted for individual susceptibility to recurrences yielded substantial residual heterogeneity.

Conclusions:

Atypical features in the clinical presentation of bipolar disorders are strongly associated with the outcome of long-term lithium treatment. Statistical models that take correlation within subjects as well as individual susceptibility into account better reflect the events during prophylactic treatment and are therefore well-suited to evaluate long-term outcome.

References:

1. Berghofer A, Kossmann B, Muller-Oerlinghausen B: Course of illness and pattern of recurrences in patients with affective disorders during long-term lithium prophylaxis: a retrospective analysis over 15 years. Acta Psychiatr Scand 1996; 93(5):349-354.
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NR111 Monday, May 22, 9:00 AM - 10:30 AM

Episodic Memory and Functional Outcome in Schizophrenia

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Educational Objectives:

At the conclusion of this session, the participant should be able to understand the concepts of and the relationship between episodic memory and functional outcome in schizophrenia. Partici-

pants will learn that episodic memory depends on the binding of contextual information. Specifically, we will emphasize the importance of the posterior right hippocampus in contextual binding. Our study used visuospatial navigation as a probe to evaluate episodic memory. The participant will learn whether visuospatial navigation is an appropriate measure of episodic memory when compared to the Wechsler Memory Scale 3rd Edition. If past experiences have not been stored within their proper context, the attempted reactivation of these experiences by relevant stimulus will appear to a schizophrenia patient as odd or strange. Clearly, this will not only impact his perception of reality, it will greatly affect his capacity to learn, ability to work, maintain social relationships and live independently. Following our presentation, participants should be able to reflect on the role of episodic memory on functional outcome in schizophrenia.

Summary:

Objective. Patients with schizophrenia exhibit impairments in episodic memory; memory for personal events encoded in a spatial and temporal context. Navigation has proven to be a useful probe to activate memory processes which are similar to those activated in the construction of episodic memory. The primary hypothesis of this study was that schizophrenia patients would show impaired performance on a navigation task when compared to a healthy control group. The secondary hypothesis was that a positive correlation exists between episodic memory and functional outcome in schizophrenia.

Methods. Participants included twenty schizophrenia patients and twenty matched control participants (16-30 years old). In the first step, after learning a navigation route, participants completed four recall tasks. They were also assessed on two tasks from the Wechsler Memory Scale, 3rd Edition (Logical Memory and Family Pictures Test) which evaluate episodic memory. In the second step, among patients, the relationship between episodic memory performance and functional outcome (social competence, school/work performance, and independent living) was examined.

Results. Replicating data previously obtained by our group, control participants performed better than schizophrenia patients on verbal ($p<.001$) and drawing recall tasks ($p<.0001$). Specifically, patients reported significantly less actions and landmarks and made more Extended Release rors in orientation changes than controls. Although patients were not impaired in identifying route landmarks, they were impaired when ranking these landmarks sequentially ($p<.001$). This corresponds to disorganization in cognitive map construction.

Conclusion. Disorganization in cognitive map construction and impairment of episodic memory are compatible with the hypothesis of hippocampal and prefrontal cortex abnormalities in schizophrenia. Preliminary data indicate that episodic memory deficit is associated with poorer functional outcome. Therefore, functional outcome in schizophrenia may be linked to hippocampal prefrontal circuit dysfunction.

References:

1. Burgess N, Maguire EA, O'Keefe J: The human hippocampus and spatial and episodic memory. Neuron 2002; 35:625-641.

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NR112 Monday, May 22, 9:00 AM - 10:30 AM

Predictors of Outcome of Depression in an Older Multi-Racial Urban Community

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Educational Objectives:

There are been few studies examining the outcome of depression in general community samples of older adults. This study examines a sample of largely indigent, predominantly black elderly persons living in a urban environment.

Summary:

Using 1990 census data for Brooklyn, N.Y., we attempted to interview all persons aged 55+ in randomly selected block groups. The initial sample consisted of 219 Caucasians and 878 Blacks. We found that 249 persons(23%) met criteria for subsyndromal or syndromal depression (CESD>7).On 2 to 3-year follow-up, 148 of these depressed persons were located and 110 were re-interviewed (mean age 68 years).The latter consisted 21% white and 79% black, of whom 23% were US born blacks, 39% were English Caribbeans, and 36 % were French Caribbeans. We examined factors that predicted continued depression on follow-up. The sample was weighted by race and gender. To control for design effects, we used SUDAAN for data analysis.

On follow-up 27% of the sample remained depressed(CESD>7). Of 10 variables entered into a logistic regression analysis, 6 variables attained statistical significance in predicting depression on follow-up: initial CESD score, race (white), worsening in daily functioning, paranoid ideation and/or psychoses, not having health entitlements, and more social contacts. Greater physical illness was marginally significant. Age, gender, anxiety level score, and lifetime traumatic events were not significant.

After several years, a majority of older community adults with depression are no longer depressed, although more than one-fourth remained depressed. Health issues - disability, number of physical disorders, and health entitlements play an important role in determining outcome

References:

1. Geerlings SW, Beekman AT, Deeg DJ, Twisk JW,Van Tillburg W: The longitudinal effect of depression on functional limitations and disability in older adults:an eight-wave prospective community-based study. Psychol Med.2001 Nov;31(8):1361-71.

2. Beekman AT,Kreigsman DM, Deeg DJ, van Tillburg W:The assosiation of physical health and depressive symptoms in the older population:age and sex differences.Soc Psychiatry Psychiatr Epidemiol,1995 Jan:30(1):32-8.

NR113 Monday, May 22, 9:00 AM - 10:30 AM

Verbal Memory Deficits in Early Psychosis: Impact on Two-Year Outcome

Rachel A. Rabin, B.S.C. *Centre for Addiction and Mental Health, Schizophrenia, 22 Northumberland Terrace, Thornhill, ON, L3T 7E5, Canada*, Jean Addington, Ph.D., Huma Saeedi, M.S.C., Donald E. Addington, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant will have learned that poor memory has an impact on social functioning in early psychosis

Summary:

Background: Cognitive deficits are a core feature of schizophrenia with one of the most consistently reported deficits being verbal memory. *Method:* Verbal memory was assessed in 107 individuals who were consecutively admitted to a comprehensive early psychosis treatment program having experienced their first episode of psychosis (FE). Subjects all had a schizophrenia spectrum disorder or other psychotic disorder. Verbal memory tasks included immediate and delayed recall of passages from the Wechsler Memory Scale, verbal learning and delayed recall of verbal

lists. Other measures included the PANSS and the Quality of Life Scale (QLS) as a measure of social functioning. A sample of 54 age and gender matched non-psychiatric controls (NPC) was also included. *Results:* There was a small but significant improvement over time for the patient groups although their scores still remained in a deficit range. Poor memory functioning was associated with positive and negative symptoms and poor ratings on the QLS at both follow-up times. There were significant longitudinal associations between QLS and memory for the controls. For the patient group poor memory functioning predicted poor QLS at both one and two year follow-ups. The FE subjects who were employed or in school at both one and two year follow-ups had superior memory functioning to those who were unemployed. *Conclusion:* First episode patients exhibit memory deficits that are consistent over time and are associated with poor social functioning and lack of employment or being in school.

References:

1. Addington, J., Saeedi, H., & Addington, D. The course of cognitive functioning in first episode psychosis: Changes over time and impact on outcome. Schiz Res 2005; 78:35-43.
2. Gold, J.M., Rehkemper,G., Binks III,S.W., Carpenter,C.J. et,al. Learning and Forgetting in Schizophrenia. J Abnormal Psychology. 2000; 109:534-538.

NR114 Monday, May 22, 9:00 AM - 10:30 AM

Gender Differences in Quetiapine Use and Response in Patients With Bipolar Disorder

Wendy Marsh, *Psychiatry and Behavioral Sciences, 401 Quarry Rd, Rm 2200, Stanford, CA 94305,* ,Terence A. Ketter, Jennifer Nam, Jennifer Culver, Anne Holland, Natalie L. Rasgon

Educational Objectives:

Participant should be able to understand mood stabilizing effect of quetiapine in bipolar disorder according to gender of patient.

Summary:

Objective:

Quetiapine (qtp) has emerging data as an antidepressant mood stabilizer in bipolar disorder and is here evaluated for the mood valence prescribed for, the dose used to treat, the effectiveness between men and women and menstrual cycle regularity in women.

Methods:

Charts of 113 qtp bipolar I, II and NOS subjects were reviewed for demographic, diagnostic, and reproductive data from the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) Affective Disorder Evaluation form. STEP-BD Clinical Monitoring Forms provided longitudinal data on mood episodes (DSM IV), qtp dose and menstrual cycles. Statistical tests include student's t-test and chi square.

Results:

Of 104 bipolar I, II and NOS subjects using qtp 67 were women and 35 men. Women were no more likely to be depressed on qtp initiation than men (p=ns). Women received a maintenance qtp dose (mg/kg) not significantly different from men. Quetiapine will be evaluated between men and women for improvement (reduction) in mood episode severity. The length and duration of menstrual cycles of reproductive age women using qtp will be presented.

Conclusions:

Given concerns regarding endocrinological health tolerability of mood stabilizers agents and the need for an antidepressant as well as antimanic mood stabilizer in one the relative lack of gender related knowledge regarding a potential new mood stabilizer like qtp, one with potential antidepressant effects needs to be addressed.

References:

1. Calabrese JR, Keck PE, Jr., Macfadden W, Minkwitz M, Ketter TA, Weisler RH, Cutler AJ, McCoy R, Wilson E, Mullen J: A randomized, double-blind, placebo-controlled trial of quetiapine in the treatment of bipolar I or II depression. Am J Psychiatry 200.
2. Rasgon N, Bauer M, Grof P, Gyulai L, Elman S, Glenn T, Whybrow PC: Sex-specific self-reported mood changes by patients with bipolar disorder. J Psychiatr Res 2005; 39(1):77-83.

NR115 Monday, May 22, 9:00 AM - 10:30 AM

Adjustment Disorders and Work Accidents

Policarpo E. Rebolledo, Sr., M.D. *Hospital del Trabajador de Santiago, Mental Health Department, Vilanova 50 Las Condes, Santiago, 6781148, Chile*

Educational Objectives:

Objetive

Describes clinical aspects of Adjustment Disorders (AD) in workers following work accidents.

Summary:

Method

Sample was selected from patients evaluated in Mental Health Department during 2004 in Hospital del Trabajador. Retrospective analysis was conducted in 303 clinical records of patients who have suffered a work accident and were referred to psychiatric assessment.

We reviewed demographic data, type of injury, psychiatric diagnoses, treatment and length of treatment.

Result

Sample of 180 men and 123 women (average 40.5 years).

In accordance with the type of accident, 29.4% were fractures, 17.8% contusions, 13.9% amputees, 9.2% traumatic low back pain and 5.9% burns.

AD represents 43% of all yearly first admission patients in Mental Health Department. 43 (14.2%) were AD with depressed mood, 91 (30%) were AD with anxious mood and 169 (55.8%) were AD with mixed anxiety and depressed mood.

Treatment was psychotherapy and pharmacotherapy in which Benzodiazepines and antidepressants were the drugs used.

The average length of treatment was 6 months.

Conclusion

Adjustment disorder is a very frequent complication in patients who have had a work accident. Current treatment is a combination of psychotherapy and pharmacotherapy.

References:

1. Adjustment disorder. Fault line in the psychiatry glossary. P. Casey, C. Dowrick and G. Wilkinson. British Journal of Psychiatry (2001, 179: 479 - 481).
2. Adult Adjustment disorder: a review of its current diagnostic status P. Casey, Journal of Psychiatric Practice (January 2001, 1: 32-40).

NR116 Monday, May 22, 9:00 AM - 10:30 AM

Folic Acid and Fluoxetine: Augmentation Pharmacotherapy and Serotonin Ssynthesis in Lymphocytes of Patients With MDD

Gustavo D. Resler, M.D. *Hospital Vargas de Caracas, Psychiatry, Av Río Caura, Residencias Parque Prado Torre 2B, Apto 111. Urb Parque Humboldt, Caracas, 1080, Venezuela,* Renée Lavie, M.D., Julio Campos, Dr. Med. Sc., Salvador Mata, Dr. Med. Sc., Mary Urbina, M.S., Lucimey Lima, Ph.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to discover new molecular mechanisms related to the fluoxetine and folate as antidepressant drugs. Also we want to show a new aproach employing lymphocytes as a model of neurochemistry.

We have the expectation to make a contribution in the psychopharmacology field, increasing the knowledge in the action mechanism of antidepressant drugs and the way that the vitamins as folic acid are related with mood disorders and its possible use as augmentation therapy.

In the other hand, we are trying to promote in our country the development of new human resources in research, occupied in the psychiatric field and laboratory investigation.

Summary:

Background: There are a number of effective interventions for the treatment of depression. It is possible that the efficacy of these treatments will be improved further by the use of adjunctive therapies such as folic acid.

Objectives: To determine the effectiveness of folic acid to augment antidepressant pharmacotherapy and its relation with 5HT synthesis and its basal levels in periferal blood lymphocytes.

Methods: 27 major depressive patients were randomly and double blind, assigned to receive during 6 weeks, 20 mg fluoxetine daily in addition to either 10 milligrams of folic acid or an identical looking placebo. Also we select 15 healthy people as control group. At the begin and the end of treatment the clinical outcome was determined with Hamilton Depression Rating Scale (HDRS) and 10 cm Visual Analogue Scale (VAS). As well, we compared the variations of plasmatic folate and homocysteine, with the intracellular lymphocyte 5HT synthesis (Vmax) and its basal concentration.

Results: The mean age of the patients was 35.04 years (range 21-58). There was no significant differences in the decrease of clinical evaluation scales between groups (p=0.8), but the folate group has a slightly improve against the placebo group, however, it was not statisticaly significant. The patients Vmax and 5HT basal levels was lower than the controls at the begin ($p \leq 0.05$), and much lower at the end of investigation. Plasmatic homocysteine levels decrease after folic acid high dose intake ($p \leq 0.05$).

Conclusions: In this investigation, folic acid was not an augmenter of standard antidepressant pharmacotherapy. The 5HT synthesis and its basal levels, decreased in depressive patients, reaches lower values after fluoxetine treatment. The medical improvement may not be due exclusively to higher 5HT intracellular levels. High dose folate intake reduce homocysteine plasmatic concentrations.

References:

1. Coppen A, Bailey J. Enhancement of the antidepressant action of fluoxetine by folic acid: a randomised, placebo controlled trial. J Affect Disord 2002; 72(3): 297-8.

2. Barton CL, Hutson PH. Inhibition of hippocampal 5HT synthesis by fluoxetine and paroxetine: evidence for the involvement of both 5HT1A and 5HT1B/D autoreceptors. Synapse 1999; 31:13-9.

NR117 Monday, May 22, 9:00 AM - 10:30 AM

Executive Function Predicts MacArthur Competency Assessment Test Scores

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Educational Objectives:

At the conclusion of this presentation, the participant should gain understanding of available bedside tests which screen for executive function impairment and of the correlation between bedside executive function screening and the MacCAT-T scores.

Summary:

Purpose: To determine whether there is a correlation between executive function and decision-making capacity and whether impairments in decision-making capacity are better detected through testing of executive functioning (via bedside testing) versus using the MacArthur Competency Assessment Test (MacCAT-T).

Methods: Twenty-one subjects, all patients over 50 expected to undergo urologic surgery, were recruited into this pilot study from a preoperative urology clinic at the South Texas Veterans Healthcare Audie Murphy Division. The MacCAT-T was administered prior to signing informed consent in order to assist with capacity assessment. Once informed consent was determined, patients were administered the Executive Interview (EXIT25), the Executive Clock Drawing Task (CLOX), and the Mini Mental State Exam (MMSE). The relationship between executive function and capacity to consent to a non-invasive research protocol using MacCAT-T were studied retrospectively.

Results: Eleven subjects passed the MacCAT-T and 10 failed. Patients who failed were more likely to be older, have fewer years education, and have worse executive function as measured by the EXIT25. There were no statistically significant differences relative to CLOX1, CLOX2, or the MMSE. The mean total MacCAT-T score for patients passing the EXIT25 (n=12, mean=17.9, SD 2.2) was significantly higher than the mean score for patients failing the EXIT25 (n=9, mean=13.6, SD 2.8) (p=0.0003). The MacCAT-T and EXIT25 were moderately correlated.

Conclusions: Given the importance of informed consent to participate in one's own treatment plan, the finding that nearly half of the patients enrolled in this study failed the MacCAT-T is concerning. The MacCAT-T is time-consuming and not used in clinical practice. If the EXIT25, which can be administered fairly quickly, could assess which patients possessed an impaired decision-making capacity, then this information could be employed by physicians to better communicate medical information with their patients.

References:

1. Grisso T, Appelbaum PS: The MacArthur treatment competence study, III: abilities of patients to consent to psychiatric and medical treatments. Law Hum Behav 1995; 19:149-174.

2. Holzer JC, Gansler DA, Moczynski NP, Folstein M: Cognitive functions in the informed consent evaluation process. J Am Acad Psychiatry Law 1997; 25:531-540.

NR118 Monday, May 22, 9:00 AM - 10:30 AM

Open-Label Study of Quetiapine in the Treatment of Fibromyalgia

Fernando Rico-Villademoros, M.D. *Biométrica, Eloy Gonzalo 27, Madrid, 28010, Spain*, Elena P. Calandre, M.D., Javier Hidalgo, M.D., Violeta Rodriguez, Juan S. Vilchez

Educational Objectives:

At the end of this presentation, the participant should be able to learn about fibromyalgia and its management.

Summary:

Introduction: Fibromyalgia is a common, disabling and difficult to treat chronic pain condition. Atypical antipsychotics may have analgesic properties (Fishbain et al 2004) and have shown some benefit in patients with fibromyalgia (Rico-Villademoros et al

2005). The aim of this study was to evaluate the potential role of quetiapine in the treatment of fibromyalgia.

Methods: This open-label study included thirty-five outpatients, >18 years, meeting the ACR fibromyalgia criteria who gave their informed consent. Quetiapine, flexibly dosed (25-100 mg/d), was added to their original treatment regimen for 12 weeks. Patients were evaluated at baseline and every four weeks using the Fibromyalgia Impact Questionnaire (FIQ) . Additionally, Beck Depression Inventory (BDI), Pittsburgh Sleep Quality Index, and SF-12 were administered at baseline and week 12.

Results: 30 (85.7%) patients (aged 47.2+7.9, 93.3% females) had a postbaseline evaluation (intent-to-treat) and completed the trial. A statistically significant reduction from baseline scores was observed in most of the analyzed scales and fibromyalgia's core symptoms, excepting pain. Regarding the magnitude of treatment effects, large effect sizes (>0.80) were observed for the FIQ-total and PSQI-total scores, while moderate effect sizes (>0.50) were encountered in the FIQ-fatigue, FIQ-stiffness, BDI-total and the SF-12 Mental Component Summary scores. Finally, small effect sizes (<0.20) were observed in the FIQ-pain and the SF-12 Physical Component Summary Score. Quetiapine was well tolerated, being the most common (>10%) adverse reactions asthenia, somnolence, nervousness, dizziness, headache, increased appetite, and pain

Conclusion: Quetiapine seems to be an efficacious and well tolerated drug for the treatment of fibromyalgia. Further randomized controlled trials are needed to confirm our results and to assess whether higher quetiapine's dose and/or longer duration of treatment might have a greater effect on pain and other outcomes.

References:

1. Fishbain DA, Cutler RB, Lewis J, Cole B, Rosomoff RS, Rosomoff HL. Do the second-generation *f*atypical neuroleptics§ have analgesic properties? A structured evidence-base review. Pain Medicine 2004; 5:359-365.
2. Rico-Villademoros F, Hidalgo J, Dominguez I, García-Leiva JM, Calandre EP. Atypical antipsychotics in the treatment of fibromyalgia: a case series with olanzapine. Progr Neuropsychopharmacol Biol Psychiatry 2005; 29:161-164.

NR119 Monday, May 22, 9:00 AM - 10:30 AM

Clinical Comparison of Patients With Bipolar Disorder With and Without Panic Attacks

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the importance of distinguishing bipolar patients with and without panic attacks.

Summary:

Objective. To compare a large group of bipolar outpatients with and without panic attacks along multiple dimensions of clinical relevance. *Method.* During a 5-year period, all new admissions to a large psychiatric outpatient clinic (N=1458) received a clinical examination, two structured interviews, and rating scales. Of the total number, 275 of the outpatients (19%) satisfied DSM-III criteria for Bipolar I disorder. Fifty-five of the 275 bipolar outpatients (27%) also met criteria for Panic attacks. *Results.* Bipolar outpatients with and without panic attacks did not differ according to gender, race, marital status, or employment status, but the group with panic attacks were younger at the time of the interview. Bipolar patients with panic attacks reported more first degree relatives with mania and sustained psychosis; however a family history of other comorbidities including suicide attempt, substance abuse, and panic attacks did not distinguish the two groups. Higher rates of psychiatric comorbidity were present among those with panic attacks including significantly more lifetime psychosis, OCD, phobia and somatization disorder, but not substance abuse. Affective symptoms had an earlier age of onset and were more severe in bipolar patients with panic disorder, especially depressive symptoms including more suicide attempts (p<.0004). No difference was noted in treatment received or recommended for these two groups. *Conclusions.* Bipolar patients with panic attacks appear to be a clinically distinct subgroup. The findings of this study suggest that all bipolar patients should be carefully screened in order to maximize treatment for those who also suffer from panic disorder.

References:

1. Chen YW, Dilsaver SC. Comorbidity of panic disorder in bipolar illness: evidence from the Epidemiological Catchment Survey. Am J Psychiatry 1995; 152 (2): 280-2.
2. Goodwin RD, Hoven CW. Bipolar-panic comorbidity in the general population: prevalence and associated morbidity. J Affect Disord 2002; 70 (1): 27-33.

NR120 Monday, May 22, 9:00 AM - 10:30 AM

Seasonality and Circadian Preference in Adult ADHD: Clinical and Neuropsychological Correlates

Yuri Rybak, M.D. *Centre for Addiction and Mental Health-Clarke Site, Mood and Anxiety, 250 College Street, Office 1163, Toronto, ON, M5T 1R8, Canada*, Heather E. McNeely, Ph.D., Bronwyn E. MacKenzie, B.A., Umesh Jain, Robert D. Levitan, M.D.

Educational Objectives:

Seasonality and Circadian Preference in Adult AD(H)D: Clinical and Neuropsychological Correlates
To consider the role of Seasonality and Circadian Preference in adults with AD(H)D and the corresponding clinical and neuropsychological correlates
To consider our findings that a delayed circadian phase disturbance contributes to both subjective and objective dysfunction in adult AD(H)D independently of mood
To consider some patients with AD(H)D as potential target candidates for chronobiological treatments such as Light Therapy (LT)

Summary:

Objective: Chronobiological disturbances are a frequent but often unrecognized contributor to AD(H)D pathology. In the current study we measured both seasonality and circadian preference in adults with AD(H)D, and their clinical and neuropsychological correlates.

Method: Thirty adult AD(H)D patients (not selected based on seasonality) were assessed in the fall-winter season using standard clinical and neuropsychological measures of AD(H)D, a depressive symptoms scale (SIGH-SAD), and two self-report chronobiological measures consisting of the Seasonal Pattern Assessment Questionnaire (SPAQ) and the Morning-Eveningness Questionnaire (MEQ). Descriptive analyses and correlations between chronobiological variables and clinical/ neuropsychological measures were performed.

Results: Consistent with our earlier report, several patients reported high degrees of seasonality with 5 of 30 (16.7%) meeting full criteria for SAD. Regarding the MEQ data (N=28), 13 subjects (46.4%) were designated as evening types, and only 4 (14.3 %) as morning types, a distribution highly discrepant with large studies of the general population. Later circadian preference was strongly

correlated with both self-reported symptoms of AD(H)D and objectively measured impulsive responding and difficulties discriminating between target and non-target stimuli. None of these findings was attributable to state depression.

Conclusions: These overall data suggest that a mood-independent delay in circadian phase contributes significantly to core pathology in many adults with AD(H)D. These findings establish a potential target for chronobiological treatments such as light therapy in this complex population.

References:

1. Levitan RD, Jain UR, Katzman MA. Seasonal affective symptoms in adults with residual attention-deficit hyperactivity disorder. Compr Psychiatry 1999;40(4):261-267.
2. Brown TE, McMullen WJ, Jr. Attention deficit disorders and sleep/arousal disturbance. Ann N Y Acad Sci 2001;931:271-286.

NR121 Monday, May 22, 9:00 AM - 10:30 AM

Severity of Depressive Symptoms is Associated to Higher Sympathetic Activity in Patients With Depression

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the positive association between depressive symptoms and sympathetic nervous system dysfunction.

Summary:

INTRODUCTION: Several pathophysiological mechanisms linking depression and higher cardiac morbidity and mortality have been identified, including autonomic nervous system dysfunction. Previous studies using indirect measures of sympathetic activity demonstrated higher sympathetic activity in depressed patients. Microneurography is a direct, secure and efficient method to measure sympathetic nerve traffic in humans. HYPOTHESIS: 1) Patients with major depressive episode have sympathetic nervous system hyperactivity, measured by microneurography; 2) Depressive symptoms are associated to an increased sympathetic modulation. METHODS: Nineteen patients with major depressive episode (32±7 years, body mass index 23±4 kg/m^2) and 15 age and body mass index-matched normal controls (32±5 years, body mass index 23±3 kg/m^2) were submitted to the Structured Clinical Interview for DSM-IV Axis I Disorders for diagnostic evaluation. Depressive symptoms were rated using the Montgomery and Asberg Depression Rating Scale (MADRS). Muscle sympathetic nervous activity (MSNA) was directly measured from the peroneal nerve using the microneurography technique. Forearm blood flow (FBF) was measured by venous occlusion pletysmography. Blood pressure (BP) was monitored by an automatic BP cuff, and heart rate (HR), by electrocardiogram. The neural and hemodynamic characteristics were evaluated at rest, during a period of 3 minutes. RESULTS: Baseline mean BP (95±12 versus 89±11, *P*=0.13), HR (76±11 versus 73±10, *P*=0.50), MSNA (24±8 versus 22±6, *P*=0.30), FBF (2.47±1 versus 2.80±1, *P*=0.30) and forearm vascular conductance (2.70±1 versus 3.17±1, *P*=0.18) were not statistically significantly different between depressed patients and normal controls, respectively. However, the levels of MSNA were statistically significantly and positively correlated with MADRS total scores (r=0.84; *P*=0.0001) and MADRS tension scores (r= 0.70; *P*=0.01). CONCLUSIONS: The severity of depressive and/or anxiety symptoms are associated to an autonomic dysfunction in depressed patients, since higher levels of MSNA were linked to higher scores of depressive and anxiety symptoms.

References:

1. Carney RM, Blumenthal JA, Stein PK, Watkins L, Catellier D, Berkman LF, Czajwoski SM, O Connor C, Stone PH, Freedland KE: Depression, heart rate variability, and acute myocardial infarction. Circulation 2001;104:2024-8.
2. Kingwell BA: Congestive heart failure/hypertension/hypertrophy: heart rate spectral analysis, cardiac norepinephrine spillover, and muscle sympathetic nerve activity during human sympathetic nervous activation and failure. Circulation 1994;90:234-40.

NR122 Monday, May 22, 9:00 AM - 10:30 AM

Runaway Adolescent Mothers: A Systematic Review of the Epidemiological Data

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Educational Objectives:

At the end of this presentation the paticipant should be able to have a review about epidemiological studies covering the theme of homeless young mothers or pregnant teens.

Summary:

Purpose: Little is known about adolescent mothers who go through pregnancy or motherhood out-of-home. This study is a review of the epidemiological literature concerning runaway adolescents mothers. *Methods*: An electronic search for original articles published from 1985 to 2004 was done. We searched for epidemiological studies including: adolescent females, pregnancy or motherhood and homeless living in out-of-home placements. *Results:* The search strategy produced 19 studies that fulfilled the selection criteria. The studies show broad heterogeneity of objectives and methods, and principally reveal that teens have high rates of: substance abuse, mental disorders, lack of social support, sexual behavior, physical and sexual violence, pregnancy, and problematic mother-child interactions. *Conclusion:* The review found few methodological rigorous articles about this specific population. Out-of-home adolescent mothers have extensive exposure to violence, drug abuse and risk of physical and mental health problems. More studies are needed in this area, especially in stigma evaluations and intervention methods for this group of women.

References:

1. Journal Article - Greene J, Ringwalt C. :Pregnancy among three national samples of runaway and homeless youth. J Adolesc Health; 23 (6), 1998, pp 370-377.
2. Journal Article-Bassuk E, Weinreb L, Buckner J et al. The characteristics and needs of sheltered homeless and low-income housed mothers. JAMA; 276(8), 1996, pp 640-646.

NR123 Monday, May 22, 9:00 AM - 10:30 AM

Sustained Attention Deficits to Facial Stimuli in Euthymic Patients With Bipolar Disorder

Syung Shick Hwang, M.D. *Anyang*, Jeong-Ho Seok, M.D., Jin Young Park, M.D., Jae-Young Chun, M.D., Duk-In Jon, M.D., Hyun-Sang Cho, M.D., See Joo Kim, M.P.H.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize sustained attention deficit in bipolar patients.

Summary:

Objective: Euthymic patients with bipolar disorder have been reported to show deficits in sustained attention. The SART(Sustained Attention to Response Task) is a kind of continous performance test and a relatively new neuropsychological paradigm that quantifies attentional Extended Release rors or slips of action. This study aimed to compare the attention capacity of euthymic bipolar patients with that of control subjects and to examine the differences in the performance of SART according to stimulus type

Method: The SART was performed to measure sustained attention capacity in 46 euthymic patients with bipolar disorder and 25 control subjects. The severity of mood symptom was assessed with 17-item Hamilton Depression Rating Scale and Young Mania Rating Scale. The efficiency estimate which reflect both the performance accuracy and speed was used as main outcome variable.

Results: There were no significant differences between both groups with regard to gender, age, or educational status. Bipolar patients showed significantly lower correct response rate in all task conditions. Efficiency estimate of the bipolar patient group was significantly lower than that of the control group. Facial stimuli related deficits were more prominent than digit stimuli related ones. However, there were no significant difference in task performance according to the facial emotion.

Conclusion: Bipolar patients showed deficit in SART even in the euthymic state. In contrast to digit stimuli, the SART using facial stimuli demonstrated prominent deficits in the bipolar patient group compared to the control group. The attention deficit of the patient group may be prominent in the more complex task condition.

References:

1. Luke Clark: Sustained attention-Deficit Confirmed in Euthymic Bipolar Disorder but Not in First-Degree Relatives of Bipolar Patients or Euthymic Unipolar Depression. BIOL PSYCHIATRY 2005;57:183-187.
2. Catherine J. Harmer: Sustained attention deficit in bipolar disorder is not a working memory impairment in disguise. Neuropsychologia 2002; 40:1586-1590.

NR124 Monday, May 22, 9:00 AM - 10:30 AM

Are There More Residual Symptoms in Psychotic Depression Than in Non-Psychotic Depression?

Montse Serra *Hospital Clínic de Barcelona, Department of Psychiatry, Villarroel 170, Barcelona, 08036, Spain*, Joana Guarch, Victor Navarro, Rosa Catalan, Rafael Penades, Cristobal Gasto

Educational Objectives:

Residual symptoms in depression

Summary:

Objective: To assess the residual symptoms and the quality of life of the unipolar major depression and to compare the prevalence and the profile of residual symptoms profile between psychotic major depression and major depression without psychotic symptoms.

Method: 37 patients with unipolar major depression were evaluated, 18 without psychotic symptoms and 19 patients with psychotic symptoms. All patients showed a endogenous depression with a Newscatle Scale up to 6 pounts and they were in a follow-up for one year. They were treated naturalistically, and they did not relapse in the last three months. All patients were evaluated with the SADS-Life (Schedule for Affective Disorders and Schizophrenia), scale of depression symptoms (Hamilton), social functioning (SASS), quality of life (QLDS) and perceived stress (PSS).

Results: There were not significant difference in the prevalence or profile of residual symptoms between psychotic and non-psychotic depression. The psychotic depression showed a significant major number of hospitalization and a significant major traits of personality Cluster A, without fullfil criteria of personality disorders. There was a significant difference in the prevalence of minor depression in non psychotic depression. The residual symptoms correlated negatively with items about quality of life and social functioning and positively with the perceived stress. Moreover, there were not difference between the number of past episodes and the overall functioning and residual symptoms between both groups, indicanting that residual symptoms could be independent of number of episodes.

Conclusion: Psychotic depression did not show more residual symptoms than the non-psychotic depression. Residual symptoms are correlated with less quality of life, less social functioning and more perceived stress. Residual symptoms did not correlate with the number of previous episodes.

References:

1. Paykel ES, Ramana R, Cooper Z, Hayhurst H, Kerr J, Barocka A. Residual symptoms after partial remission: an important outcome in depression. Psychol Med 1995; 25:1171-1180.
2. Judd LL, Akiskal HS, Maser JD, et al. A prospective 12-year study of subsyndromal and syndromal depressive symptoms in unipolar major depressive disorders. Arch Gen Psychiatry 1998; 55:694-700.

NR125 Monday, May 22, 9:00 AM - 10:30 AM

Stress During Pregnancy and Its Impact on the Newborn

Alison Shea, M.S. *St. Joseph's Healthcare, Women's Health Concerns Clinic, 50 Charlton Ave East, 6th Floor, Fontbonne Bldg., Hamilton, ON, L8N 4A6, Canada*, Alison Fleming, Ph.D., Mark Kamath, Ph.D., David Streiner, Ph.D., Meir Steiner, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should become familiar with certain phyiological measures that can be used to identify stress vulnerability among pregnant women and gain some insight as to how stress-related changes in physiology may affect the developing fetus.

Summary:

Stress, anxiety and depression during pregnancy are associated with adverse infant outcomes, but the specific mechanisms and effects on infant development remain largely unknown. **Objective:** To study the underlying physiological mechanisms related to prenatal maternal adversity. **Methods:** Pregnant women (14-24 weeks gestation) are being recruited from a study taking place at the Women's Health Concerns Clinic, St. Joseph's Healthcare, Hamilton. Women with depressed/ anxious symptoms are offered a choice of treatments/ interventions (adversity group). Healthy women with no current or past psychiatric illness are recruited for comparison. Baseline assessment includes: Mini International Neuropsychiatric Interview; family history; Childhood Trauma Questionnaire; Montgomery and Asberg Depression Rating Scale (MADRS); Hamilton Anxiety Rating Scale (HAM-A); Edinburgh Postnatal Depression Scale (EPDS); Spielberger State-Trait Anxiety Inventory (STAI). Morning salivary samples are collected for measurement of stress indicators (cortisol, DHEA, alpha amylase (AA)). A follow-up assessment is completed at 24-30 weeks and includes: MADRS, EPDS, HAM-A, STAI, salivary samples, and a 24-hour Holter electrocardiogram. Infants will be followed during the postpartum period, till three years of age. **Results:** Preliminary results (n= 41) indicate that AA levels (sympathetic nervous sys-

tem (SNS) measure) are positively correlated with anxiety scores during pregnancy, while morning cortisol levels were negatively associated with depression and anxiety scores ($p<0.05$). The cortisol awakening response was lower for adversity subjects versus controls ($p<0.05$). Maternal 24-hour mean heart rate during pregnancy was negatively correlated with infant head circumference at birth, controlling for birth weight and gestational age ($p<0.01$). **Conclusions:** The SNS and the HPA axis may be affected in opposite directions by stress/ depression/ anxiety during pregnancy. Increased SNS tone may affect normal fetal growth. Understanding the physiological mechanisms involved in maternal responses to stress may contribute to early intervention strategies.

References:

1. Field T, Diego M, Hernandez-Reif M, Schanberg S, Kuhn C, Yando R, Bendell D. Pregnancy anxiety and comorbid depression and anger: effects on the fetus and neonate. Depress Anxiety. 2003;17:140-51.
2. Van den Bergh BR, Mulder EJ, Mennes M, Glover V. Antenatal maternal anxiety and stress and the neurobehavioural development of the fetus and child: links and possible mechanisms. A review. Neurosci Biobehav Rev. 2005;29:237-58.

NR126 Monday, May 22, 9:00 AM - 10:30 AM

Non-Medical Influences on Psychiatric Hospitalization

Kathleen A. Sheehan, M.S.C. *University of Oxford, Department of Psychiatry, Department of Psychiatry, Warneford Hospital, Oxford, OX3 7JX, United Kingdom*, Tom Burns, D.Sc.

Educational Objectives:

Understand the balance between clinical and non-clinical pressures on psychiatric hospital admission. Know the state of current literature on the subject. Recognize the value of ascertaining patient expectations.

Summary:

Background: Medical decision-making is often driven by factors other than clinical need. Research in family practice confirms the importance of clinicians' perception of patient expectation, however little is known about its role in psychiatry. This study describes the pressures, beyond medical need, experienced by clinicians during the in-patient admissions process.

Methods: 140 consecutively admitted patients were interviewed. The admitting clinician in each case was sent a questionnaire about the process. 46% of the questionnaires were returned, allowing for analysis of 64 patient-clinician dyads.

Results: Clinicians reported that they felt pressure, beyond simple medical need, to admit the patient to hospital in 19/64 cases. 35 patients stated that they wanted to be admitted to hospital, whereas clinicians judged that the patient wanted admission in 42 cases. Overall clinicians correctly assessed the patient's wishes in 49 cases. When views were incongruent, clinicians were twice as likely to consider that the patient wanted admission when this was not the case. Correct patient-clinician agreement on wanting admission was significantly associated with higher therapeutic alliance as rated by the patient (Helping Alliance Questionnaire: 2.6 v. 1.9, $t=2.76$, $p<0.01$).

Conclusions: Nearly one-third of clinicians felt that their decision to admit a patient to hospital was influenced by factors beyond medical need. Pressure from the patient's family and the patient themselves were the most common of these factors. Although clinicians accurately assessed patients' attitudes to admission in 76% of cases, they tended to overestimate patients' desire to be admitted. The association between congruence of views and higher therapeutic alliance score could suggest that actively ascertaining patients' views regarding treatment options may enhance the patient-clinician relationship.

References:

1. Engleman NB, Jobes DA, Berman AL, Langbein LI: Clinicians' decision making about involuntary commitment. Psychiatr.Serv. 1998; 49:941-945.
2. Little P, Dorward M, Warner G, Stephens K, Senior J, Moore M: Importance of patient pressure and perceived pressure and perceived medical need for investigations, referral, and prescribing in primary care: nested observational study. BMJ 2004; 328:44.

NR127 Monday, May 22, 9:00 AM - 10:30 AM

Functional Genetic Polymorphisms and the Response to Treatment for Bipolar Depression

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Educational Objectives:

At the end of this presentation the participant should be able to (i) recognize the difficulty of predicting response in the treatment of bipolar depression, (ii) describe proposed effects of genetic polymorphisms and the response to pharmacotherapy in bipolar depression, in particular the serotonin transporter, 5-HT2A receptor and p-glycoprotein polymorphisms, and (ii) understand how allelic variations in serotonin transporter may help predict clinical response.

Summary:

Objective: Patients with bipolar disorder spend the majority of their symptomatic times depressed, and the pharmacological treatment of bipolar depression often involves a process of trial and Extended Release ror, with few clinical and/or biological predictors of response. Pharmacogenetics provides a potential tool in identifying genetic predictors of response, thus improving the treatment of bipolar depression.

Method: This randomized, double-blind study involved bipolar depressed outpatients recruited from a tertiary-care hospital setting. Sixteen patients entered the study and received add-on treatment with either citalopram or lamotrigine to their regular mood stabilizer medication(s). Patients were followed for 12 weeks and assessed using the 17-item Hamilton Depression Scale (Ham-D), Montgomergy Asberg Depression Rating Scale (MADRS) and Young Mania Rating Scale (YMRS). Genetic testing was completed to determine each patient's genotype for the 5HT transporter, 5-HT2A receptor and p-glycoprotein MDR1 3435T/C and 2677G/T/A polymorphisms. Reduction in total MADRS score was the primary measure of improvement.

Results: The results showed that the short allele of the 5HT transporter polymorphism was significantly associated with poorer response, independent of the treatment medication. The results for the remaining polymorphisms did not reach statistical significance.

Conclusions: As described in previous literature, the 5HT transporter gene appears to be an important locus affecting treatment response. The results from this study suggest a potential means to predict the response to treatment for patients suffering from bipolar depression.

References:

1. Rybakowski JK, Suwalska A, Czerski PM, et al: Prophylactic effect of lithium in bipolar affective illness may be related to

serotonin transporter genotype. Pharmaco. Rep. 2005; 57:124-7.

2. Zanardi R, Serretti A, Rossini D, et al: Factors affecting fluvoxamine antidepressant activity: influence of pindolol and 5-HTTLPR in delusional and nondelusional depression. Biol. Psychiatry 2001; 50:323-330.

NR128 Monday, May 22, 9:00 AM - 10:30 AM

Somatization in Russian and Hispanic Immigrants

Paulo Rinaldo Shiroma, M.D. *Maimonides Medical Center, Psychiatry, 914 48th Street, Brooklyn, NY, 11219*, Milton Kramer, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the multiple factors that may alter the intensity of somatic complaints. These will include the acculturation process and the demographic variables.

Summary:

Objective: To investigate 1) the prevalence of somatization among Russian and Hispanic immigrants;2) the relationship between acculturation and somatization; and 3) whether demographic factors alter the intensity of somatic complaints.

Method: Hispanic origin patients, 115 and Russian origin patients,52 were studied for somatization and acculturation in a psychiatric clinic. The patients were chronically ill and suffering from mood disorders and/or psychosis. We defined somatoform symptoms by score on the somatization subscale of the Symptom Check List Revised 90. Acculturation level was measured by a short acculturation scale. Demographic data was collected, including age, gender, marital status, occupation, country of origin, time in the U.S. and educational level.

Results: a) Somatization was significantly higher among Russian immigrants [mean=1.45(+/-0.7)] than Hispanic immigrants [(mean=1.12(+/-0.86)] ($p<0.02$);b) Acculturation level was significantly higher among Hispanic immigrants [mean= 1.83(+/-0.62)] than Russian immigrants [mean=1.6(+/-0.69)] ($p<0.05$);c) The length of stay in the US correlated with acculturation level in Hispanics immigrants($r=0.23$, $p<0.02$) and Russian immigrants($r=0.47$, $p<0.001$);d) The length of stay was significantly higher among Hispanic immigrants[mean=29.99(+/-13.64)] than Russian immigrants[mean=12.7(+/-7.21)] ($p<0.001$);e) There is a relationship between the educational level and ethnicity(chi-square= 54.03,$p<0.001$) as 82% of Russians immigrants had completed high school compared with 22% of Hispanic immigrants.

Conclusions: Russian immigrants have higher somatization scores and lower acculturation scores than Hispanic immigrants. Apparently the length of time in the new country is the major factor related to the degree of acculturation as the Russians with lower acculturation scores have been in the US a shorter period of time. The educational level and the length of time in the new country could account for some of the difference in somatization.

References:

1. Escobar JI: Somatization in the community. Arch Gen Psychiatry 1987; 44: 713-718.

2. Angel R, Guarnaccia PJ: Mind, Body and Culture: Somatization among Hispanics. Soc Sci Med 1989; 28: 1229-1238.

NR129 Monday, May 22, 9:00 AM - 10:30 AM

Heavy Drinking in the São Paulo Epidemiologic Catchment Area Study in Brazil: Gender and Socio-Demographics Correlates

Camila M. Silveira, M.D. *FMUSP, Section of Psychiatric Epidemiology - LIM 23 - Department and Institute of Psychiatry, Rua do Rocio, 423, cjto 1209, vila olímpia, Sao Paulo, 04552-000, Brazil*, Yuan-Pang Wang, Ph.D., Arthur G. Andrade, Ph.D., Laura Andrade, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to:

1. Get information about heavy drinking, a harmful pattern of alcohol consumption related to acute or chronic health problems and social consequences.
2. Recognize the magnitude of heavy drinking pattern in the São Paulo Epidemiologic Catchment Area Study in Brazil.
3. Verify the effect of gender, age, and other sociodemographic factors in this population.
4. Be able to compare the findings with data from other countries.

Summary:

Objective: The main objective of this study was to quantify heavy drinking (HD) among adults living in a defined Catchment Area in the city of São Paulo-Brazil, and analyzed the effect of gender, age, and other sociodemographic factors.

Method: Data were from the São Paulo Catchment Area study. A representative sample (N= 1,464) of the adult population living in two boroughs of the city of São Paulo were assessed through CIDI 1.1. The pattern of lifetime and 12-month alcohol consumption was evaluated. An algorithm for heavy drinking in the previous year was developed considering quantity and frequency of drinking. Prevalence rates and socio-demographic correlates were examined separately for men and women.

Results: The overall 12-month prevalence of HD in this sample was 13.5% with 18.9% of men and 9.4% of women reporting HD. Sixty per cent of the women and 28.9% of men were lifetime abstainers. The odds of heavy drinking for women were increased for those 18-44 years of age and for those who were not married (separated, divorced, widowed and never married), while among men, the major risk factor was never being married.

Conclusions: The rates of HD for both gender were higher in these two middle-class boroughs than those reported in others Brazilian studies. HD also was common among women and not confined to the younger groups. Intervention program and preventive campaign should focus high-risk population. Future prospective studies are needed to assess the impact of heavy alcohol use on health, mental health and social functioning.

Key words: alcohol use disorders; alcohol; heavy drinking; gender; demographic correlates; prevalence; general population; Brazil

References:

1. Webb CP, Bromet EG, Gluzman S, Tintle NL, Schwartz JE, Kostyuchenko S, Havenaar J M. Epidemiology of heavy alcohol use in Ukraine: findings from the world mental health survey. Alcohol & Alcoholism 2005; 40(4):327-35.

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NR130 WITHDRAWN

NR131 Monday, May 22, 9:00 AM - 10:30 AM

The Perceived Needs of Psychiatry Residents Regarding the Physician-Manager Role

Sanjeev Sockalingam, M.D. *University of Toronto, Psychiatry, 80 St Clair Avenue East Apt. 1909, Toronto, ON, M4T 1N6, Canada*, Vicky Stergiopoulos, M.D., Julie D. Maggi, M.D.

Educational Objectives:

At the conclusion of this presentation, participants will be aware of existing gaps in psychiatry resident training in the physician-manager role. They will be able to identify the knowledge and skills areas where residents perceive the greatest gaps with regards to their current residency training. Participants should be able to appreciate the need to consider the perceived needs of psychiatry residents in the development of a physician-manager curriculum.

Summary:

Objective: The Royal College of Physicians and Surgeons of Canada highlights the importance of the physician-manager role. Despite this emphasis, resident education in the area is limited. This study attempts to determine psychiatry residents' perceived current and desired knowledge and skills and educational preferences regarding a physician-manager curriculum.

Methods: An 11-question survey was mailed to 102 University of Toronto psychiatry residents. The residents were asked to rate their current and desired level of knowledge and skill in selected areas of administrative psychiatry. Educational preferences on teaching methods were also obtained. The main outcome measures were gap scores (GS), the difference between resident desired and perceived current knowledge (GS_k) or skill (GS_s) rating. Data was analyzed using descriptive statistics and multiple linear regression.

Results: The response rate was 48% (n = 49). Calculated mean knowledge gap scores were largest for physician compensation, program planning, quality improvement, health care reform, organizational structures and program evaluation. Mean skill gap scores were greatest for self and career development and leading change. Multiple linear regressions revealed that the total scores for individual GS_k and individual GS_s were not associated with gender, training level, past administrative experience, past medical administrative education or advanced degrees. Workshops, small group and mentorship learning methods were each preferred by greater than 60% of respondents.

Conclusion: Successful development of a physician-manager curriculum will require that the perceived needs of residents and their preferred educational methods of teaching be considered. This study suggests that psychiatry residents identify significant gaps in several knowledge and skill areas relating to the physician-manger role, with most perceived deficits relating to the individual and program level.

References:

1. Somers JL, Goldner EM, Leseage AD, Fleisher WP, Leverette JS: Filling gaps in psychiatric education: skills in administrative psychiatry and knowledge of mental health systems, services and policy. Can J Psych (insert) 2004; 49(6):1-6.
2. Yu-Chin R: Teaching administration and management within psychiatric residency training. Acad Psychiatry 2002; 26(4):245-52.

NR132 Monday, May 22, 9:00 AM - 10:30 AM

Hippocampal Volume in PTSD: Meta Analysis

Shabnam Sood, M.D. *Maricopa Integrated health system, psychiatry, 3429 East Norcroft Circle, Mesa, AZ, 85213*, Dawson W. Hedges, Kathleen Mathieson, Ph.D.

Educational Objectives:

Posttraumatic stress disorder, a chronic disorder, is characterized by autonomic hyperarousal, intrusive memories and flashbacks. Recently, some but not all studies have reported smaller hippocampal volumes in people with posttraumatic stress disorder compared to controls, although the nature of the relationship between reduced hippocampal volume and posttraumatic stress disorder remains unknown. Moreover, differences between studies concerning the type of trauma (e.g., combat versus assault) as well as differences between control groups have further impeded the interpretation of the available studies. Small sample sizes in many of these studies add yet another confounding factor, predisposing them to type II errors. To better characterize the published volumetric hippocampal studies in PTSD, we performed a meta-analysis on published studies of hippocampal volume in posttraumatic stress disorder.

Summary:

PTSD is associated with reduced hippocampal volume compared to controls. In order to characterize the relationship between hippocampal volume and PTSD, we performed a meta-analysis of published studies of hippocampal volume in PTSD. Method: Pubmed and PsychINFO databases were searched for articles with PTSD and hippocampal volume assessed via magnetic-resonance imaging. Reference tables of articles were reviewed for additional studies. Articles that included hippocampal volumetric data from MRI studies of PTSD groups and control groups were included, regardless of the type of trauma or whether control groups had been exposed to trauma. Based on the data in the identified articles,we compared average right and left hippocampal volumes between patients with no history of trauma, patients with trauma history but no PTSD and patients with PTSD. Results:Subjects in 13 identified studies with no history of trauma had significantly larger right (mean adjusted effect size delta=0.62;95% CI:0.33, 0.90; p=0.0000) and left (mean adjusted effect size delta= 0.65;95% CI:0.37,0.95; p=0.000)hippocampal volumes compared to patients with PTSD. In contrast, there were no significant differences in right and left hippocampal volumes between trauma patients witn no PTSD and patients with PTSD(mean adjusted effect size delta=0.42; 95% CI:-0.11, 0.97; p=0.06 and mean adjusted effect size delta=0.19; 95% CI: -1.91, 2.29; p-0.42, respectively). Conclusions: These findings support the notion that PTSD is associated with reduced hippocampal volume regardless of the type of trauma. However, the lack of a significant difference between the hippocampal volumes in patients exposed to trauma but without PTSD and patients with PTSD suggests that trauma exposure itself may be associated with hippocampal volume reduction. As such, these findings indirectly may address the etiology of some of the volume reduction found in PTSD in that a critical factor for hippocampal volume loss may be trauma exposure and not necessarily the development of PTSD.

References:

1. Bremner JD, Randal P, Vermetten E,et al:Magnetic resonance imaging based measurements of hippocampal volume in patients with combat related PTSD. Am J Psychiatry1995; 152:973-981.
2. Boone O, Brandes D, Giloba A, Et al:Longitudinal MRI study of hippocampal volume in trauma survivors with PTSD. Am J Psychiatry 2001;158(8):1248-1251.

NR133 Monday, May 22, 9:00 AM - 10:30 AM

The Psychosocial and Physical Response to Menarche Among Female Adolescent Earthquake Victims in Taiwan

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the psychosocial and physical response to menarche among female adolescent earthquake victims. He should also be able to describe the association of earthquake

exposure and negative impact on female adolescent's response to manarche.

Summary:

Introduction: The exposure to nature disaster may have long-term impact on adolescent's mental health in several aspects. We investigated the impact of Taiwan 921 earthquake on female adolescent's psychosocial and physical response to menarche.

Methods: 355 female adolescents in a rural area in middle Taiwan were assessed with self-rated questionnaires three years after the earthquake. The basic epidemiological data, experience of exposure to the earthquake, Moos menstrual stress questionnaire, emotional response to menarche scale, and self-efficacy scale were collected. The other 176 control subjects in a non-exposure area in north Taiwan also completed the same questionnaires.

Results: The mean age of adolescent victims was 12.5 years and in the 5th to 8th school grade range. They had more humiliation feeling toward menarche. Their autonomic symptoms and face flushing during menstrual period were more severe. The earthquake's destructive effect to life and subjective threatening perception were associated with negative psychological and physical response to menarche.

Conclusions: This study demonstrated that exposure to a major earthquake had negative impact on female adolescent's response to menarche. Psychological support and heath education about menarche and menstruation were recommended to these earthquake victims.

References:

1. Tahirovic HF: Menarche age and the stress of war: an example from Bosnia. Eur J Pediatr 1998; 157:978-980.
2. Koff E, Rierdan J: Preparing girls for menstruation: recommendations from adolescent girls. Adolescence 1995; 30:795-811.

NR134 Monday, May 22, 9:00 AM - 10:30 AM

The Comparison of Temperament and Character Traits of Vitiligo and Chronic Urticaria in Patients with Healthy Controls

Meltem Sukan, M.D. *Mardin State Hospital, Psychiatry, Mardin State Hospital, Mardin, Turkey*, Fulya Maner, M.D., Kemal Sayar, M.D.

Educational Objectives:

At the conclusion of the presentation, temperament and character may play a role in the onset, exacerbation or chronicity of skin disorders.

Summary:

Introduction: The aim of the study was to examine the temperament and character features of two different kinds of skin disorders, vitiligo and chronic urticaria, and make a comparison with healthy controls.

Methods: The sample was 50 vitiligo, 50 chronic urticaria patients recruited from dermatology clinics at four major hospitals in Istanbul, from February 2003 till December 2004. The patient groups were compared with age- and sex- matched 50 healthy controls. All subjects underwent Cloninger's Temparement and Character Inventory and the Turkish version of the Structured Clinical Interview for DSM-IV Mental Disorders.

Results: The scores of sentimentality, compassion versus revengefulness, creative self-forgetfulness, spritual acceptance, self-transcendence were higher in vitiligo and chronic urticaria groups than controls. On the other hand, the scores of dependence, responsibility, purposefulness, resourcefulness, congruent second nature, empathy, integrated conscience of the control group were higher than the patient groups. The scores of dependence and congruent second nature, and transpersonal identification were found higher in chronic urticaria group than vitiligo group.

Conclusion: The temperament features represent the individual differences in character and skills. The relationship between the precipitating psychological factors and the alterations in the psychological state after skin disorders occured are being issues to be investigated. In this area temperament and character may have an important role.

References:

1. Cloninger, CR, Przybeck TR, Svrakic DM, Wetzel RD. Temperament and Character Inventory (TCI): A Guide to Its Development and Use. Washington University School of Medicine, Department of Psychiatry, St Louis, MO; 1994.
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NR135 Monday, May 22, 9:00 AM - 10:30 AM

Belief Disparities in Anxious Children

Shifali Arora, B.A. *Chicago, IL*, Lina Sweiss, B.A., Patricia Graczyk, Ph.D., Sucheta Connolly, M.D.

Educational Objectives:

Educational Objective

At the conclusion of this presentation, the clinician should be able to recognize a distinction between a child's beliefs and behavior routine. When dealing with children with anxiety disorders, the family's established norms, morals and interactions must be taken into consideration. Considering that children model their behavior after their parents, their beliefs may actually be contradictory due to abnormal levels of anxiety. This is, therefore, an important concept that should be addressed. It is possible that the children and parents see their current situation very differently, thus allowing us room to explore the implications behind this.

Prior studies investigated the biological and psychological implications along with social consequences, but few investigated the familial and social aspect as a dimension. This study shows the disparity that exists between the family's set norms and beliefs and that of the anxious child. After looking at this study, clinicians will be aware of one more component in which further attention is necessary to help improve the quality of life of these children.

Summary:

An Insufficient number of studies have researched the association between behavior routines and beliefs in families with clinically anxious children. Studies have focused on one or two specific factors dealing with families, but few have looked at the whole picture including social interactions and communication (Dadds, Heard & Rapee, 1992). To bridge this gap, our first hypothesis states a lack of association exists between children's beliefs and behavior within the family infrastructure based on the Family Relationship Scale (FRS). Our second hypothesis states a lack of association exists between children's beliefs and their primary caregiver's beliefs, consequently feeding into disruption within family interactions. As was found by Peleg-Popko (2002), a significant negative correlation existed between the parents and child's level of communication, encouragement of personal growth, and system maintenance. Our third hypothesis states an association exists between children's primary anxiety diagnosis to their beliefs and behavior routines.

Method

Patients were asked to participate in this research for University of Illinois' Institute for Juvenile Research by completing consent forms and the FRS (children N=53; parents N=64). Paired t-tests were completed for hypothesis one; Independent t-tests for hy-

pothesis two; and one-way ANOVA for hypothesis three. The patient population was divided into two age groups; 5-11 and 12-18 years old.

Results

Preliminary results revealed one significant negative correlation between beliefs and behavior routines (r=-.358, p=.031) amongst the five to 11-year-old children.

Implication

Showing only one significant finding may be a result of a low participation rate. Nonetheless, the significant negative correlation found suggests a dichotomy exists between anxious children's value/belief system and their actions. Accordingly, the clinician should not ignore the possibility that their patient may show disparities in what they think and how they act.

References:

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2. Peleg-Popko O: Children's test anxiety and family interaction patterns. Anxiety, Stress & Coping 2002; 15:45-59.

NR136 Monday, May 22, 9:00 AM - 10:30 AM

Depression and Its Correlates in Patients With Kidney Transplants

Lilla Szeifert *Semmelweis University, Institute of Behavioral Sciences, Nagyvarad ter 4., Budapest, 1089, Hungary*, Miklos Zsolt Molnar, M.D., Agnes Zsofia Kovacs, Csaba Ambrus, M.D., Andras Szentkiralyi, M.D., Istvan Mucsi, M.D., Marta Novak, M.D.

Educational Objectives:

The prevalence of depression after successful kidney transplantation, although significantly lower than in waitlisted dialysis patients, is still high and it may be associated with poor outcome. Transplanted patients should be regularly assessed for psychological distress and treated if indicated.

Summary:

Introduction: The prevalence of depression is 15%-50% among patients with end-stage renal disease. There is only very little information available on the epidemiology of depression in kidney transplanted patients. **Methods:** 1067 kidney transplanted (Tx) and 214 waitlisted dialysis (WL) patients have been approached to participate in our cross-sectional study, 854 Tx and 176 WL patients agreed to participate (participants). Baseline demographic characteristics, treatment data and laboratory results were collected from medical documentation. The patients completed a battery of self administered, validated questionnaires including the Center for Epidemiological Studies-Depression (CES-D) scale. **Results:** Mean age of patients was 49±12 years, 60% of patients were male, the prevalence of diabetes was about 17% in both groups. The prevalence of depression was significantly higher in WL versus in Tx patients (41% versus 27%; p<0.001). The prevalence of depression was significantly higher in women than in men (31% versus 23%; p<0.01). Tx patients with depression had significantly worse kidney function than patients without these symptoms. In a multivariate logistic regression model serum albumin (a marker of overall clinical condition) and self-reported financial situation were significantly and independently associated with the presence of depressive symptoms in the Tx group (p=0.042 and p<0.001, respectively). **Conclusion:** The prevalence of depression after successful kidney transplantation, although significantly lower than in waitlisted dialysis patients, is still high and it may be associated with poor outcome. Transplanted patients should be regularly assessed for psychological distress and treated if indicated.

Grants: OTKA TS 040889, OTKA T038409, NKFP 1/002/2001, ETT 218/2003, TeT Foundation (2005/06, MN), Hungarian Eotvos Scholarship (MN).

References:

1. Kimmel PL: Depression in patients with chronic renal disease: what we know and what we need to know. J Psychosom Res 2002; 53:951-956.
2. Baines LS, Joseph JT, Jindal RM: Emotional issues after kidney transplantation: a prospective psychotherapeutic study. Clin Transplant 2002;16:455-460.

NR137 Monday, May 22, 9:00 AM - 10:30 AM

The Association of Restless Legs Syndrome With Depression in Patients With Kidney Transplants

Andras Szentkiralyi, M.D. *Institute of Behavioural Sciences, Semmelweis University, Budapest, Psychonephrology Workgroup, 6 Aranykut st, Budapest, H-1172, Hungary*, Istvan Mucsi, M.D., Anett Lindner, Rezso Zoller, M.D., Agnes Koczy, Miklos Zsolt Molnar, M.D., Marta Novak, M.D.

Educational Objectives:

Our results suggest that restless legs syndrome (RLS) is correlated with a higher score on the CES-D scale, which indicates an increased risk for clinically significant psychological distress.

Summary:

Background: There is a bidirectional association between insomnia and depression in patients with chronic medical conditions. RLS is a frequent movement disorder in renal patients, is associated with chronic insomnia and we hypothesized that it may be associated with depressive symptoms, as well.

Methods: In a cross-sectional study, 1067 kidney transplanted patients (Tx) were asked to complete a battery of questionnaires. Laboratory data were extracted from patients' charts, basic sociodemographic data were recorded at enrollment. The patients completed a battery of self administered, validated questionnaires including the Center for Epidemiological Studies Depression (CES-D) scale, the Restless Legs Syndrome Questionnaire and the Athens Insomnia Scale (AIS). A cut-off score of 16 on the CES-D was used to identify patients with potentially significant depression.

Results: 80% of patients approached completed all the questionnaires. Mean age was 49±13 years, 59% was male and 17% had diabetes. Patients with RLS had significantly higher CES-D scores than those without the syndrome (median[interquartile range] 16[15] versus 9[12], p<0.001) and the prevalence of depression was also higher in the RLS group (54% versus 25%, p<0.001). We found a moderately strong, significant correlation between the AIS and CES-D scores (R=0.521; p<0.001). In a multivariate regression model, the presence of RLS was a significant, independent predictor of the CES-D score (p=0.001) after adjusting for important co-variables (age, gender, albumin, comorbidity, estimated GFR). After entering the AIS score in the model, the presence of RLS was no longer significantly associated with the CES-D score.

Conclusion: The presence of RLS is associated with depression in kidney transplanted patients. This association could be mediated by chronic insomnia induced by RLS.

Grants: OTKA TS 040889, OTKA T038409, NKFP 1/002/2001, ETT 218/2003, TeT Foundation (2005/06, MN), Hungarian Eotvos Scholarship (MN).

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insomnia and quality of life in patients on maintenance dialysis. Nephrol Dial Transplant 2005; 20:571-577.

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NR138 Monday, May 22, 9:00 AM - 10:30 AM

The Essential Drugs Programme in Gauteng, South Africa: Implementation in the Public Sector Mental Health Service

Rita G. Thom, Prof. Dr. *University of the Witwatersrand, Psychiatry, 7 York Rd, Parktown, Johannesburg, 2193, South Africa*

Educational Objectives:

At the conclusion of this presentation, participants will have an understanding of the implementation of the Essential Drugs Programme in mental health services in Gauteng, a densely populated, urbanised province in South Africa.

Summary:

Objectives:

To review expenditure on psychotropic medication in Gauteng province, South Africa over a number of years.

To highlight implications in terms of the policy of developing community mental health services and deinstitutionalising mental health care.

Methodology:

Expenditure on psychotropics was reviewed for the financial years: 2001/2; 2002/3 and 2003/4. Analysis of expenditure in hospital and district health services was carried out.

Results:

Between 4.49% and 5.72% of total drug expenditure was spent on psychotropic medication. Almost two-thirds of this was spent in the district mental health service. The cost/patient/day in the district mental health service was in line with the 6% inflation rate in South Africa at the time (approximately 0.25 to 0.27 US dollars).

Gauteng is the only province in South Africa that had permission to use the atypical antipsychotic (risperidone).There has been significant concern from health service managers about the direct acquisition costs of risperidone. Results of this review show that there was an increase in expenditure on risperidone in both hospital and district mental health services in 2002/3 when this medication became more freely available, but that this decreased slightly in 2003/4.

Conclusions:

Newer generation psychotropic medications do increase the direct acquisition costs for health services. However, this has not been excessive in Gauteng province in South Africa. The expenditure review shows that the policy of developing community mental health services is being implemented at least in terms of providing medication in the district health service. Further research needs to be carried out on the pharmacoeconomic benefit of using newer generation medications over cheaper older medications.

References:

1. World Health Organisation: Promoting rational use of medicines: core components. WHO Policy Perspectives on Medicines. World Health Organisation. September 2002. World Health Organisation. Geneva.

2. Csernansky JG, Mahmoud T, Brenner R. : A comparison of risperidone and haloperidol for the prevention of relapse in patients with schizophrenia. N.Engl.J.Med 2002;3;346(1):56-8.

NR139 Monday, May 22, 9:00 AM - 10:30 AM

Obstructive Sleep Apnea in Patients With Severe Persistent Mental Illness

Anthony M. Tobia, M.D. *University of Medicine and Dentistry of New Jersey, Psychiatry, University Behavioral Health Care-Dayton Office, 2245 Route 130, Suite 106, Dayton, NJ, 08810-1413*, Katie Hilton, M.A., Carol Brooks, R.N., Mohammed Siddiqui, M.D., Mark D. Miceli, M.D., Anita Mallya, M.D.

Educational Objectives:

At the conclusion of this session, the participant should have an increased awareness of the prevalence of obstructive sleep apnea (OSA) in the mentally ill, appreciate the risk factors associated with this disorder, and understand a systematic method to assess patients with the complaint of excessive daytime sleepiness.

Summary:

Background:A recent study demonstrated that Obstructive Sleep Apnea(OSA) was associated with an increased risk of stroke and death for any cause, independent of other risk factors. Current psychopharmacological treatment for severe mental illness includes agents that are known to cause sedation and weight gain-risk factors for the development of OSA. Despite this, there is a lack of research of OSA in this special population.

Objective: To study the prevalence of OSA in patients with severe persistent mental illness attending a partial hospital program.

Methods: The complaint of excessive daytime sleepiness (EDS) in adults with severe persistent mental illness attending a partial hospital program will be examined in a systematic manner. Gender, age, weight, body mass index (BMI), neck circumference, blood pressure, current medications, Epworth Sleep Scale score, psychiatric and medical diagnoses and use of alcohol and/or other illicit substances will be recorded for each patient with EDS. Patients will be referred to a sleep specialist for polysomnography and evaluation for OSA.

Results: The factors described above will be correlated with the results of polysomnography. Odds ratios of receiving a diagnosis of mild, moderate or severe OSA will be calculated for each variable, including psychiatric diagnosis and current medication. The prevalence of OSA in patients with EDS will be calculated.

Conclusions: There is a lack of research of OSA in mentally ill populations. Given the impact of OSA on mortality and the propensity of current psychiatric medications to cause sedation and weight gain, psychiatrists need to take a lead role in facilitating the diagnosis and treatment of this condition in their patients.

References:

1. Yaggi, HK, et al.: Obstructive Sleep Apnea as a Risk Factor for Stroke and Death. N Eng J Med 2005; 353(19): 2034-2041.

2. Caples, SM, et al.: Obstructive Sleep Apnea. Ann Intern Med. 2005; 142: 187-197.

NR140 Monday, May 22, 9:00 AM - 10:30 AM

Gender-Specific Cytokine Expression in the Brain of Victims of Suicide

Leonardo H. Tonelli *University of Maryland, Psychiatry, 685 West Baltimore Street, MSTF Building Room 502, Baltimore, MD, 21201*, Dan Rujescu, M.Psy., Teodor T. Postolache

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the importance of allergies as a possible triggers for suicide. The specific gender effect of allergies in women as triggers for depression and suicide. And to raise awearness that treating allergies is very important in clinical practice.

Summary:

Introduction: Inflammatory cytokines (TH1) exacerbate depression and may precipitate suicide in vulnerable individuals. Considering that allergy is associated with depression[1] and possible suicide[2] in women, we are analyzing the relative expression of TH1 *vs* TH2 (allergy related) cytokines in regions of the brain implicated in suicide, and comparing women and men.

Methods: Total mRNA obtained from orbitofrontal cortex from 61 individuals (age: 53.9 SD: 16.9), with 33 suicides (15 women and 28 men), and 18 controls (6 women and 12 men) was used to perform real-time RT-PCR to quantify interleukin-1β, interlukin-2, 4 and 6 and interferon-γ. Main effects and interactions of cause of death and gender were analyzed with ANOVAs.

Results: A significant gender*suicide interaction was found for interleukin-1β/interleukin-4 ration ($p<0.05$), with lower values of IL-1β and higher IL-4 in suicide females. No differences were observed in the other cytokines analyzed to date.

Conclusion: A decreased interleukin-1β/interleukin-4 ratio is consistent with the association between allergy and depression in women[1] and our previous report of increased suicide rates in women during the allergy season[2].

References:

1. Timonen M, Jokelainen J, Silvennoinen-Kas sinen S, Meyer-Rochow VB, Herva A, Rasanen P: Atopy and depression: results from the Northern Finland 1966 Birth Cohort Study.
2. Postolache TT, Stiller JW, Herrell R, et al: Tree pollen peaks are associated with increased suicide in women. Mol Psychiatry 2005; 25:45-57.

NR141 Monday, May 22, 9:00 AM - 10:30 AM

Differences Between Bipolar I and II Patients Regarding Neurocognitive Performance

Carla Torrent *Hospital Clinic, Rosselló 140, Barcelona, 08036, Spain*, Anabel Martinez-Arán, Claire Daban, Mercè Comes, Jose Sánchez-Moreno, Benedikt Amann, Eduard Vieta

Educational Objectives:

At the conclusion of this presentation, the participant should be able to identify the cognitive performance in bipolar II patients and to recognize the role of the neuropsychological performance in the psychosocial functioning in bipolar II patients.

Summary:

Introduction: Persistent impairments in neurocognitive function have been described in patients with bipolar disorder whose disease is in remission. So far, no studies have been performed to identify the specific differences regarding neuropsychological performance when bipolar I and bipolar II subtypes are compared.

Methods: A sample of 71 euthymic bipolar patients (38 bipolar I, 33 bipolar II), were included in the study. Euthymia was defined by a score of 6 or less at the Young Mania Rating Scale, and a score of 8 or less at the Hamilton Depression Rating Scale, for at least six months. The bipolar I and II patients were compared on several clinical and neuropsychological variables and the two groups were contrasted with 35 healthy controls on cognitive performance.

Results: The two groups showed significant deficits in most cognitive tasks compared to healthy controls. After controlling for age, bipolar I patients performed worse than bipolar II patients in all neurocognitive measures. However, the bipolar II group showed a trend towards a higher number of perseverative Extended Release rors in the Wisconsin Card Sorting Test compared to the bipolar I group, but differences did not reach statistical significance.

Conclusions: Cognitive impairment exists in both subtypes of bipolar disorder, although it is most evident in the bipolar I group. Bipolar II patients seem to show an intermediate profile regarding neurocognitive performance between bipolar I and healthy controls.

References:

1. Zubieta JK, Huguelet P, O'Neil RL, Giordani BJ. Cognitive function in euthymic bipolar I disorder. Psychiatry Res 2001; 102: 9-20.
2. Fleck DE, Shear PK, Strakowski SM: Processing efficiency and sustained attention in bipolar disorder. J Int Neuropsychol Soc 2005; 11: 49-57.

NR142 Monday, May 22, 9:00 AM - 10:30 AM

Insight in Schizophrenia: Assessment of 31 Patients With Different Scales

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to know different types of scales can be used to assess insight in schizophrenia. Moreover, he should link insight impairment and the Frith theory on schizophrenia in which attribution impairment is the main dysfunction.

Summary:

Insight is more than frequently altered in schizophrenia. Two different types of scales can be used to assess consciousness: self-questionnaires directly filled by the patient or questionnaires filled by a psychiatrist after an interview.

The aim of this study was first to assess insight in schizophrenic patients using these two different types of scales and then try to find out a link between insight impairment and schizophrenic symptoms. The self-questionnaire was the Self Appraisal of Illness Questionnary (Marks et al.), 17 items finally giving four scores (consciousness of illness, consequences of schizophrenia, need for treatment and worries about illness) plus a total score of insight. The other questionnaire was the Scale for assessment of Unawareness of Mental Disease (Amador) consisting in an interview with a psychiatrist who finally assesses four dimensions (consciousness of illness, symptoms, need for treatment and consequences of illness) plus a total score. Moreover, Amador's scale enables to measure how much the patient relates symptoms to his illness.

31 patients - half of them being outpatients - whose schizophrenia diagnosis had been previously made according to D.S.M.IV criterions were evaluated. Drugs prescriptions were controlled, all of the patients being medicated with an antipsychotic, a benzodiazepine and a sleep inducer. They were all assessed by the two scales previously mentioned and the Positive and Negative Syndrome Scale (Kay et al.).

Total scores of insight scales were significantly correlated ($p<.001$). For each questionnaire, the four different scores were independent from each other ($p<.001$). No correlation was found between insight scales and schizophrenic symptoms intensity. Considering symptoms attribution, we found a link between being unconscious of a symptom and being unable to attribute it to schizophrenia were linked, which could refer to the Frith theory of schizophrenia and attribution impairment as a main dysfunction.

References:

1. Marks K.A., Fastenau P.S., Lysaker P.H. et al.: Self-Appraisal of Illness Questionnaire (SAIQ): relationship to researcher-rated insight and neurophysiological function in schizophrenia. Schizophr Res 2000; 45 : 203-11.

2. Amador X.F., Strauss D.H.: The scale to assess Unawareness of Mental Disorder (SUMD). Columbia University and New-York State Psychiatric Institute 1990.

NR143 Monday, May 22, 9:00 AM - 10:30 AM

Peer-Facilitated Psychoeducation for BPD

Kiera A. Van Gelder, M.A. *Middle Path, 147 Summer St., #11, Waltham, MA, 02452*, Kim Kay Holt, B.A.

Educational Objectives:

At the conclusion of this session, the participant should be able to:

a. Understand the psychosocial interventions used in this model;

b. Identify the benefits and limitations of peer-facilitated support for borderline personality disorder;

c. Recognize the value of educating consumers with BPD on their illness as a means of reducing stigma and empowering individuals to take control of their symptoms.

Summary:

This presentation discusses the development of a peer-facilitated psychoeducation model for individuals who have been diagnosed with BPD and who have achieved a level of stability through professional intervention but continue to experience distress around symptoms related to their illness.

The model relies on Dr. Perry Hoffman's definition of psychoeducation as "a modality of treatment for a specific illness that includes engagement, education, coping skills training along with a set of guidelines for recovery and maintenance in conjunction with problem solving techniques for either illness, family stabilization or both" (Hoffman, 2005).

The Borderline Peer Recovery Skills Group (BPRS) utilizes peer facilitators to educate consumers on BPD using a support group format interwoven with practices from Mary Ellen Copeland's Wellness Recovery Action Plan (WRAP) and Dr. Marsha Linehan's Dialectical Behavior Therapy (DBT). The aims of the group include stigma reduction, increasing self-management skills, illness education, and the development of a wellness plan for relapse prevention and, in the case of increased care, for self-direction and engagement with mental health professionals.

Developers of this program will present outcomes of 2 12-week pilot groups and discuss strategies for implementing this model in outpatient treatment and community settings.

References:

1. Hoffman PD, Fruzzetti AE: Psychoeducation. In The American Psychiatric Publishing Textbook of Personality Disorders. edited by Oldham J, Skodol A, Bender D, American Psychiatric Press Inc, 2005.

2. Lequesne ER, Hersh RG: Disclosure of a Diagnosis of Borderline Personality Disorder. Journal of Psychiatric Practice 2004; 10(3):170-176.

NR144 Monday, May 22, 9:00 AM - 10:30 AM

The Relationship Between Ethnicity and Pain Perceptions

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that there may be a unique relationship between ethnicity and pain perception which may be independent of socioeconomic, educational, or marital variables.

Summary:

Background:

Previously it has been suggested that ethnicity may play a role in pain perception. But it is difficult to isolate the effect of ethnicity on pain perception when socioeconomic, educational, and marital variables are so variable. There is a need to better delineate the relationship between ethnicity and pain experience.

Objective:

To examine the relationship between ethnicity and pain perceptions.

Study Design/Measurements:

Subjects who were matched for educational, socioeconomic, and marital status were selected from a cohort who met DSM-IV diagnostic criteria for schizophrenia spectrum disorder at New Jersey Veteran Administration System(n = 18) who did not have cognitive deficits precluding participation. The McGill Pain Questionnaire-SF was used to assess multidimensional pain experience. Associated psychotic and depressive symptoms were measured using PANSS and HAM-D scales respectively. The data was analyzed using descriptive statistics.

Results:

18 subjects rated the pain of living with psychotic illness using the McGill Pain Questionnaire. The subjects were divided into African American(9) and Caucasian groups(9) to assess the relationship between ethnicity and pain perceptions. African American patients had PANSS average score of 75.9 with McGill (affective & evaluative) score of 9.9 and HAM-D score of 4.6. Caucasian patients had PANSS average score of 63.3 with McGill(affective & evaluative) score of 10 and HAM-D score of 2.9.

Discussion:

Ethnicity may have a role in modulating pain experience in a subset of patients. African American patients reported less subjective pain (McGill-SF) in presence of more psychotic symptoms (PANSS). 2 groups were matched for socioeconomic, educational, and marital variables. These findings suggest there may be an independent effect of ethnicity on pain experience and tolerance as it relates to the level of distress in dealing with a psychotic illness.

References:

1. American Pain Society. Guidelines for the treatment of pain. JAMA 1995;274:1870-8.

2. Melzack R. The McGill Pain Questionnaire. In: Pain Measurement and Assessment. New York:Raven Press, 1983, 41-48.

NR145 Monday, May 22, 9:00 AM - 10:30 AM

The Development of a District Branch Website: www.tennpsych.org

Susannah T. Williams, M.D. *University of Tennessee, Psychiatry, 788 South Cox, Memphis, TN, 38104*, Kristin S. Beizai, M.D.

Educational Objectives:

At the conclusion of this presentation, participants will gain a comprehensive understanding of the content of all nationwide APA district branch websites, and the steps required to use this information to inform website design. Participants will be shown images of a new district branch website created by this method.

Summary:

Professional advocacy for psychiatrists involves participation in public events, raising awareness of mental illness, and political lobbying. Historically, physicians have been reluctant to participate in politics on an individual level (Rothman, 2000). Physician advocacy has been shown to be most effective when taking the form of collective action, and collective action is considered the hallmark of professionalism (Gruen et al., 2004). In Tennessee, the percent-

age of psychiatrists who are members of the American Psychiatric Association (APA) is only 45.2%. Notable current issues facing Tennessee psychiatrists include a recurrent psychologist prescribing bill, and recent changes to TennCare (the state Medicaid managed care program), such as patient disenrollment and formulary restrictions. To mount an effective response to legislative issues such as these, organized and rapid communication of information within the association is absolutely required. In recent years, the APA and the majority of the district branches have increased communication though the use of websites. However, the various district branch websites differ extensively in content. This project has two main objectives: first, quantification and analysis of the information contained within each of the 43 APA district branch websites; second, utilization of this information for the design and creation of a website for the Tennessee Psychiatric Association, www.tennpsych.org. Images of this new website, and initial statistics of user access will also be presented.

References:

1. Rothman DJ: Medical professionalism--focusing on the real issues. N Engl J Med 2000; 342(17):1283-1286.
2. Gruen RL, Pearson SD, Brennan TA: Physician-citizens--public roles and professional obligations. JAMA 2004; 291(1):94-8.

NR146 Monday, May 22, 9:00 AM - 10:30 AM

Relationships Between Past Alcohol Abuse and Dependence, and Cognitive and Psychological Symptoms Among Currently Outpaients With Depression

Janet M. Witte, M.D. *Massachusetts General Hospital, Psychiatry, 7 Whitman St, Somerville, MA, 02144*, Amy H. Farabaugh, Ph.D., Maribeth Pender, Ph.D., John J. Worthington III, M.D., Maurizio Fava, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to identify a number of cognitive and psychological symptoms which do and do not characterize currently depressed persons with past history of alcohol abuse/dependence.

Summary:

Introduction: A substantial number of patients with current MDD have a past history of alcohol abuse/dependence (AA/D); it is unclear if these patients have distinct psychological and cognitive traits compared to patients with current MDD without a past history of AA/D. The aim of this study is to evaluate the possible relationship between past AA/D and specific cognitive and psychological symptoms among depressed outpatients. **Methods:** 169 depressed outpatients (99 women, 70 men; mean age 40.5 + 10.6 years) were enrolled in a treatment study of depression. At baseline, they met criteria for MDD based on the SCID-P, and were administered the self-rated Symptom Questionnaire (SQ, with depression, hostility and anxiety scales), the Perceived Stress Scale (PSS), the Cognitions Questionnaire (CQ), and the Dysfunctional Attitudes Scale (DAS). Patients with AA/D in the past 12 months were excluded. The multiple linear regression method was used to examine the relationship between each symptom and the lifetime diagnosis of AA/D, adjusting for severity of depression. **Results:** 51 (30%) patients reported a past history of AA/D. Significantly ($p<.05$) higher SQ hostility scores were associated with past history of AA/D compared to depressed patients without a history of AA/D (mean score: 13.3 + 6.2 versus 11.3 + 6.4), while there were no significant differences in SQ anxiety, PSS, CQ, and DAS scores between these two groups. **Conclusion:** Outpatients with MDD and past history of AA/D report higher levels of anger/hostility than depressed outpatients without such history, but do not appear to have significant differences in cognitive symptoms, such as dysfunctional attitudes and perceived stress levels. Further studies exploring the nature of this relationship are warranted, as well as the study of these traits among depressed patients currently abusing alcohol.

References:

1. Fava M, Davidson K, Alpert JE, Nierenberg AA, Worthington J, O'Sullivan R, Rosenbaum JF. Hostility changes following antidepressant treatment: relationship to stress and negative thinking. Journal of Psychiatric Research 1996; 30(6): 459-467.
2. Fava M, Farabaugh AH, Sickinger AH, Wright E, Alpert JE, Sonawalla S, Nierenberg AA, Worthing JJ 3rd. Personality disorders and depression. Psychological Medicine 2002; 32(6):1049-57.

NR147 Monday, May 22, 9:00 AM - 10:30 AM

The Influence of Group Psychoeducation Course on Improving Volunteers Stigma Attitude Toward Mental Illness in a General Hospital

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to demonstrate the importance of hospital volunteers in the anti-stigma action of mental illness both in community and hsopital. They should also be able to recognize the influence of psychoeducation course on improving volunteers' stigma attitude toward mental illness.

Summary:

Introduction: Stigma attitude toward mental illness has severe impact on psychiatric patients' work and life, even their human right. Studies have been conducted in different culture environments to evaluate the stigma attitude and how to change it, mostly the subjects were health care professionals and students. Volunteers in hospital are often willing to help others and have influence in their community. It is important to improve their stigma attitude to have benefit toward psychiatric patients. This study investigated the influence of psychoeducation course on improving volunteers' stigma attitude toward mental illness in a general hospital

Methods: 102 volunteers in a general hospital were recruited. They were randomly assigned to either experimental or control group. Experimental group subjects attended two hours lecture and one hour group discussion course about community psychiatry and psychiatric rehabilitation. Control group subjects attended general education course. The attitude to mental illness scale was completed before, immediately after, and after one month of education course by both groups. Data analysis using repeated measures ANCOVA were performed to compare the differences in these two groups.

Results: The mean age of the 51 subjects in experimental was 42.5 years, most of them were married and had high school education. The complete rate of questionnaires immediately after and after one month were 100% and 76.5%. Comparison of the groups indicated that significant improvement of some domains of stigma attitude in the experimental group subjects were detected, both immediately after and after one month of education course.

Conclusions: The results of this study showed that our educational course has both short-term and mid-term effects in improving volunteers' stigma attitude. The limitation of our study is the relatively short intervention times and lack of variety in teaching materials and methods. Whether long-term effect exists still need longer observation and follow up.

References:

1. Chen M, Jang HR, Chen CC: The influence of psychiatric lectures and nursing internships on attitude toward psychiatric illness in nursing students. Chinese Psychiatry 1991; 5: 151-158.
2. Yen CF, Chong MY: Attitude toward mental illness: a study of change during psychiatric internship. Taiwanese J Psychiatry 1998;12: 64-72.

NR148 Monday, May 22, 9:00 AM - 10:30 AM

Prevalence and Correlates of ADHD: School-Based Mental Health Services in Korea

Su-Jin Yang *Chonnam National University Hospital, 5 Hakdong, Dong-ku, Kwangju, 501-746, Republic of Korea*, Juyeon Lee, Sunyoung Kim, Haewon Cheong, Seongshim Cheong, Sungdo Hong, Kyungsun Noh

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that prevalence of ADHD in Korea. And the ADHD were associated with male, family enviornment, and lower academic achievement.

Summary:

Objectives: To estimate the prevalence and correlates of children who had ADHD in Seoul, Korea.

Methods: A cross-sectional survey of 2,429 children included in four elementary schools at Seoul. Parents and teachers completed the Korean ADHD Rating Scales (K-ARS) and the Korean version of the Strengths and Difficulties Questionnaire (SDQ-Kr). Child psychiatrists interviewed the children who demonstrated clinically significant scores on K-ARS and SDQ-Kr. Further assessments were conducted with other psychological tests if needed.

Results:

1. Of 2,429 children, 158 (6.5%) children had ADHD.

2. Compared to controls, ADHD children showed more frequently male preponderance, more single parent family, lower parental education level, more paternal no employment, poorer sibling relationship, fewer number of friends, and lower ability in language and mathematics.

3. In multivariate analysis, ADHD were associated with boys, single parent family, poor sibling relationship, and low language ability. Our stratified analysis by gender, there were association with single parent family and lower language ability in boys, and poor sibling relationship and lower mathematics ability in girls.

Conclusions: This study found 6.5% prevalence of ADHD and ADHD were associated with gender, family environment, and academic achievements. Understanding of high-risk children would help in developing an ADHD school mental health program in Korea.

References:

1. Rahman A, Mubbashar M, Harrington R, Gater R: Annotation: developing child mental health services in developing countries. J Child Psychol Psychiat 2000; 41:539-546.
2. Sanford MN, Offord DR, Boyle MH, Peace A, Racine YA: Ontario child health study: social and school impairment in children aged 6 to 16 years. J Am Acad Child Adolesc Psychiatry 1991; 31:60-66.

NR149 Monday, May 22, 9:00 AM - 10:30 AM

The Korean Version of Schizophrenia Quality of Life Scale: Testing the Reliability and Validity and Its Relationship With PANSS

Seon-Jin Yim, M.D. *Seoul Natonal Hospital, Psychiatry, Department of Psyhciatry, Seoul National Hospital, 51 Neungdong-Ro, Gwangin-Gu, Seoul, 143711, Republic of Korea*, Jin-Hun Kim, M.D., Sungkil Min, Ph.D., Seungup Kim, M.D., Diane J. Wild, M.D.

Educational Objectives:

New Schizophrenia Quality of Life Scale released, cross cultural validation and its relationship with PANSS. This would be very interesing and educative to all psychiatists.

Summary:

Objectives : Schizophrenia Quality of Life Scale(SQLS-R4) is the revising version of SQLS. The instrument evaluates quality of life in patients' point of view, considering the changes caused by atypical antipsychotics. This study was performed to verify the validity and value of the revision 4th of Schizophrenia Quality of Life Scale(SQLS-R4) as an assessment tool in a Korean-language version (KSQLS-R4).

Methods : The subjects for present study were 196 patients with a diagnosis of schizophrenia as defined by DSM-IV. The KSQLS-R4 was administered together with self-report Korean version of WHOQoL-BREF to assess concurrent validity. Psychotic symptoms and general functioning were evaluated using the PANSS and the GAF score respectively. A subset of respondents also completed the KSQLS-R4 for a second time to assess test-retest reliability. KSQLS-R4 consists of 33 items, asking experiences in the past week. Score for each item ranges from 0 to 4 by the frequency. The total score ranges from 0 to 100, and the lower the total score the higher the quality of life of the subject.

Results : All the scales of KSQLS-R4 showed good internal consistency reliability (Cronbach's alpha= 0.859). The correlations of items with their scale total revealed that almost all items were significantly correlated with their own scale score. There was relevant association between WHOQOL-BREF sub-scores and KSQLS-R4 score total. Also relevant or moderate correlations between PANSS, current GAF and KSQLS-R4 were proved.

Conclusion : From the results of the testing the reliability and validity of the KSQLS-R4, it is concluded that the KSQLS-R4 is a simple and reliable scale for measuring quality of life in schizophrenic patients.

References:

1. Darren J Claysona, Diane J Wild, Helena A Doll, Colin R Martin and Marc De Hert. The revision and psychometric re-validation of the Schizophrenia Quality of Life Scale. Unpublished paper. (In Press).
2. Wilkinson G, Hesdon B, Wild D, Cookson R, Farina C, Sharma V, et al. Self-report quality of life measure for people with schizophrenia: the SQLS. British Journal of Psychiatry 2000;177,42-46.

NR150 Monday, May 22, 9:00 AM - 10:30 AM

Body Mass Index Changes in Children and Adolescents Taking Aripiprazole: Retrospective Review

Robert Zalewski-Zaragoza, M.D. *Naval Medical Center San Diego, Mental Health, 1316 Surftide Lane, San Diego, CA, 92154*, Robert McLay, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the effect of aripiprazole on the body mass index of children and adolescents.

Summary:

Objective: To evaluate the risk of weight gain in children and adolescents taking aripiprazole.

Methods: A review of outpatient records for those individuals who where prescribed aripiprazole from 2003-2005 at the Child

and Adolescent Clinic at the Naval Medical Center San Diego. Age, sex, initial heights and weights, time of trial, along with concomitant medications were recorded. A pre and post body mass index (BMI) was calculated. Patients taking other atypical antipsychotics or who took aripiprazole for less than 30 days were excluded.

Results: A total of 56 records were included in the analysis. The mean length of trial was 222 days. Overall, there was a mean increase in BMI of 1.02 (SE=0.64, p=0.0005). Sex, age, initial BMI and length of trial did not have a statistical effect on the change of BMI. Use of stimulants (slope 7.3, p=0.003) and whether or not the patients were switched from another atypical (slope -1.6, p= 0.004) did correlate with changes. Concomitant use of stimulants actually showed an increase in BMI (mean change 2.08 p=0.006). For those who recently changed from a different atypical there was a mean decrease in BMI (mean change -1.1, p=0.295). Lastly, for those not on stimulants or recently switched from another atypical there was not a significant change in BMI (mean change = -0.40, p=0.34).

Conclusions: Aripiprazole by itself does not confer an increase in BMI in children and adolescents. Switching from another atypical to aripiprazole tends to lower BMI. Use of aripiprazole while on stimulants has the interesting effect of increasing BMI. The mechanism is not known but it may be blocking the know weight loss effect of stimulants.

References:

1. Kelly DL, Conely RR, Love RC, Horn DS, Ushcahk CM. Weight gain in adolescents treated with risperdone and conventional antipsychotics over six months. J Child Adolesc Psychopharmacol 1998; 8:151-159.
2. Patel NC, Kistler JS, James EB, Crismon ML. A retrospective analysis of the short-term effects of olanzapine and quetiapine on weight and body mass index in children and adolescents. Pharmacotherapy. 2004; 24(7):824-30.

NR151 Monday, May 22, 1:00 PM - 2:30 PM

Both Hypocortisolaemia and Hypercortisolaemia Are Associated With Major Depression in Late Life

Marijke A. Bremmer, M.D. *VUMC medical Center, psychiatry, LASA, Boechhorststraat7, Amsterdam, 1081 BT, The Netherlands*, Dorly JH Deeg, Prof. Dr., Aartjan TF Beekman, Prof. Dr., Brenda WJH Penninx, Ph.D., Paul Lips, Prof. Dr., Witte JG Hoogendijk, Prof. Dr.

Educational Objectives:

At the conclusion of this presentation the participant should be able to understand the functioning of the Hypothalamo-Pituitary-Adrenal (HPA) Axis in late-life depression. The talk will focus on changes in functioning of the HPA-axis that occur with aging and how how both hyporeactivity and hyperreactivity of the HPA-axis might be associated with late-life depression. New data from the Longitudinal Aging Study Amsterdam will be presented.

Summary:

In younger people depression has been associated with a hyperactivity of the HPA-axis and hypercortisolaemia. However, McEwen supposes that a longstanding adaptation to stresses, either physical or mental, could lead to a wear and tear of neuronal systems and to a hypo-reactivity of the HPA-axis. Therefore, we examined whether in older age there is a U-shaped association between depression and cortisol, indicating both hypoactivity as well as hyperactivity of the HPA-axis.

Methods: data from 1219 participants of the Longitudinal Aging Study Amsterdam, aged 65 and over. Respondents using oral corticosteroids were excluded. Both subthreshold depressive disorders and major depression were assessed. Plasma concentrations of cortisol (CORT) and Corticosteroid Binding Globuline (CBG) were determined and from these (CORT/CBG) a Free Cortisol Index (FCI) was computed. The presence of a U-shaped association was tested using both the continuous levels of FCI and the squared term FCI^2 in logistic regression analysis. Correction was made for chronic diseases.

Results: there was a U-shaped association between FCI and major depression (B FCI = -0.361 (SE 0.164) p=0.027; B FCI^2= 0.013 (SE 0.006) p=0.022). The same results were found for the association between CORT and major depression (B CORT= -9.20 (SE 4.07) p=0.024; B $CORT^2$=0.008 (SE 0.004) p=0.031). Respondents with cardiovascular diseases and cognitive decline had significantly higher FCI levels (p=.004 and p=<.001 resp.) Conclusion: in older people both hypocortisolaemia and hypercortisolaemia are associated with major depression. Hypercortisolaemic depression is associated with cardiovascular diseases.

References:

1. McEwen BS: Protective and damaging effects of stress mediators. N Engl J Med 1998 338: 171-179.
2. Oldehinkel et al: Urinary free cortisol secretion in elderly persons with minor and major depression. Psychiatry Res 2001; 104:39-47.

NR152 Monday, May 22, 1:00 PM - 2:30 PM

Exploration of Biological Markers of Suicidal Behavior in MDD

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Educational Objectives:

Most suicides (about 90%) occur in the context of psychiatric disorders. Prediction of suicide risk in patients with mental illness is very important in preventing suicide attempts. However, current approaches to predict suicidality are based on clinical history and have low specificity and biological markers are not yet included. Many studies have explored the association between different biological parameters, such as serotonin, cholesterol and suicidality. In our study, new candidate biological markers such as nitric oxide, neurotrophins, cytokines were measures in depressed patients with suicidal attempt.

BDNF, NO, and cytokines are considered to have high predictability of biological factors for major depressive disorder.

Summary:

Most suicides occur in the context of depressive disorders Prediction of suicide risk in patients with major depression is very important in preventing suicide attempts. However, current approaches to predict suicidality are based on clinical history and have low specificity and biological markers are not yet included. So, we explored the biological markers for the suicidal behaviors in major depressive disorders.Suicidal subjects consisted of 48 patients (18 males and 30 females) admitted to emergency rooms following suicide attempts between August 2003 and November 2005. Nitric oxide, BDNF, IGF-1, NGF, TGF-beta1 were measured in the plasma of suicidal depressed patients and age-, sex matched normal controls. TNF-alpha, IFN-gamma, IL-2, IL-4, IL-6 were measured in culture supernatant after mitogen stimulation of whole blood in both groups. Hamilton Depression Rating Scale, Lethality of Suicide Attempt Rating Scales, and Risk-Rescue Rating System were measured in the suicidal patients. The levels of nitric oxide, IL-6, and TGF-beta1 were increased in the suicidal patients comparing with the normal controls, while the levels of BDNF, IFN-gamma, IL2, IL-4 were decreased in the patients. The levels of IGF-1, NGF and TNF-alpha were not different between suicidal patients and normal controls. Discriminant analysis

showed that IL-4, IL-2, TGF-beta1, BDNF, and IL-6 have relatively high predictability of biological factors for major depression. These results suggest that BDNF, cytokines and nitric oxide would be new biological markers in suicide behavior in major depression. The longitudinal study is needed to find out the change in the blood levels of the biological markers and clinical changes in depressive patients.

References:

1. Kim YK, Myint AM (2004): Clinical application of low serum cholesterol as an indicator for suicide risk in major depression. Journal of Affective disorders 81: 161-166.
2. Myint AM, Leonard BE, Steinbusch HM, Kim YK (2005): Th1, Th2, Th3 cytokines alterations in major depression. Journal of affective disorder Oct 88(2) 167-173.

NR153 Monday, May 22, 1:00 PM - 2:30 PM

Brain-Derived Neurotrophic Factor Polymorphisms and Schizophrenia: Association Study in a Chilean Sample

Aida Ruiz, M.D. *Universidad de Chile, Avenida La Paz 1003, Santiago, Chile*, Pak Sham, M.D., John Powell, Eduardo Miranda, M.D., Robin M. Murray, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to understand genetic association analysis of complex disorders

Summary:

Objective: A growing body of evidence suggests that brain - derived neurotrophic factor (BDNF) gene, on chromosome 11p13, is associated with schizophrenia. The objective of this study was to evaluate the possible association between BDNF gene and susceptibility to this disorder in a Chilean schizophrenic sample.

Method: Forty- four affected families, according to DSM-IV criteria, were collected in Santiago, Chile. Four SNPs previously reported to be associated with schizophrenia and other psychiatric disorders were genotyped. The pedigree disequilibrium test (PDT) was used to estimate linkage disequilibrium (LD) between markers, and to test single marker and haplotype association. The PDT was performed using the PDTPHASE program

Results: No significant significant allelic association between the four BDNF SNPs and illness was found ($P > 0.05$). Tests for haplotype analysis showed no association ($P > 0.05$).

Conclusions: The results of this study do not support an association between these BDNF genetic variants and genetic risk for schizophrenia in this Chilean sample.

References:

1. Hall D, Dhilla A, Charalambous A, Gogos A, Karayiorgou M: Sequence variants of the brain-derived neurotrophic factor (BDNF) gene are strongly associated with obsessive 'compulsive disorder. Am J Genet 2003; 73:370-376.
2. Shoval G, Weizman A: The possible role of neurotrophins in the pathogenesis and therapy of schizophrenia. Eur Neuropsychopharmacol 2005; 15:319-329.

NR154 Monday, May 22, 1:00 PM - 2:30 PM

Polymorphisms of MAO and COMT Genes in Koreans With Schizophrenia

Kyoung-Uk Lee *Gyeonggi-Do*, Hoo-Rim Song, Chi-Un Pae, Jeong-Jin Kim, Hae-Kook Lee, Yong-Sil Kweon, Chung Tae Lee

Educational Objectives:

At the conclusion of this presentation, the participant should be informed that the genetic variations of the MAOA genes might contribute to the risk for schizophrenia

Summary:

We investigated the hypothesis that the genetic variation of genes encoding monoamine oxidase (MAO) and catechol-O-methyl transferase (COMT) might be related to the susceptibility to schizophrenia. We genotyped the 941 T/G and the promoter 30-bp variable nucleotide tandem repeat (VNTR) polymorphisms in the monoamine oxidase A (MAOA) gene, A/G polymorphism in intron 13 of the monoamine oxidase B (MAOB) gene and V158M polymorphism in the COMT gene in schizophrenic patients (n= 180) and control subjects (n=136). Significant differences of allele distribution in the MAOA VNTR polymorphism for female gender were observed between patients and controls ($p<0.05$). Also, there was a significant differences in the allele distribution of MAOA 941T/G polymorphism when combined ($p<0.05$). No significant differences of genotypic and allelic distributions for either gender alone or when combined were observed between patients and controls for A/G polymorhism in intron 13 of MAOB and V158M polymorphism in the COMT gene. In the test of additive effects, no significant differences were observed between patients and controls.

This study suggested that the genetic variations of the MAOA genes might contribute to the risk for schizophrenia in some Korean populations. However, polymorphisms of MAOB and COMT genes may not play a role in the pathogenesis of schizophrenia.

Keywords: Schizophrenia; Monoamine oxidase; Catechol-O-Methyl Transeferase; Polymorphisms

References:

1. Norton, N. et al. Schizophrenia and functional polymorphisms in the MAOA and COMT genes: no evidence for association or epistasis. Am J Med Genet., 2002:114;491-496.
2. Park, TW. et al. Functional catechol-O-methyltransferase gene polymorphism and susceptibility to schizophrenia. Eur Neuropsychopharmacol. 2002:12:299-303.

NR155 Monday, May 22, 1:00 PM - 2:30 PM

Are Early Visual Processing Deficits Endophenotypic for Schizophrenia? High-Density Electrical Mapping Study in Clinically Unaffected, First-Degree Relatives

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognise that the main aim of this study is to establish an endophenotypic marker for schizophrenia using electrophysiological techniques. They should understand the concept of an endophenotype i.e. a quantifiable measure of risk for a disorder and why it is important in the identification of high risk individuals. They would be aware of the presence of marked early visual processing deficits, mainly demonstrated by a very impaired P1 component, in patients with schizophrenia as well as their clinically unaffected first-degree relatives compared to controls. An easily measured and readily identifiable component, the P1 component is a good candidate for an endophenotypic marker.

Summary:

Background: In schizophrenia, one of the most promising avenues for establishing endophenotypes lies in recordings of the

event-related potential (ERP) where robust early visual processing deficits have been shown. The visual 'P1' component has consistently been found to be impaired in patients. This effect is very strong with the P1 amplitude in patients less than half the strength seen in healthy controls.

Objective: To investigate whether the visual P1 deficit is also observed in first-degree unaffected relatives and to establish its potential role as an endophenotypic marker for schizophrenia.

Methods:

Subjects: 25 (15 female) healthy first-degree biological relatives of known patients with schizophrenia (DSM-IV) were recruited. Control subjects comprised 26 (13 female) paid volunteers. All participants were free of any psychiatric illness and on no medication.

Stimuli: Subjects were presented with approximately 100 isolated check images and 40 line drawings of 2 kinds of animal on a white background in a random order. They completed between 10-15 blocks each lasting 3 minutes. Only ERPS to standard checkerboard stimuli were analysed.

Data acquisition & Analysis: Continuous EEG was acquired from 72 scalp electrodes on Biosemi system and analysed using BESA. The MANOVA was calculated on SPSS.

Results: There was a significant and highly robust main effect of group ($p=0.004$) indicating substantially reduced P1 amplitude in the first-degree relative group compared to controls. The deficit was localised largely to the midline regions in early visual sensory cortices and dorsal visual stream. The effect size ($d=0.9$) was large over these scalp sites.

Conclusions: This is the first study to show that clinically unaffected first-degree relatives also have significant impairments in early visual processing as indexed by the P1. This observation is found in the absence of any age, gender or medication effects, strongly suggesting that it is associated with genetic risk for schizophrenia.

References:

1. Foxe JJ, Doniger GM, Javitt DC: Early visual processing deficist in schizophrenia: impaired P1 generation revealed by high-density electrical mapping. Neuroreport 2001; 12:3815-20.
2. Butler PD, Zemon V, Schecter I et al: Early-stage visual processing and cortical amplification deficits in schizophrenia. Arch Gen Psychiatry 2005;62:495-504.

NR156 Monday, May 22, 1:00 PM - 2:30 PM

Reasons for No-Show to Initial Substance Abuse Treatment in Psychiatric Comorbids

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Educational Objectives:

At the conclusion of this session, the participant will understand factors involved in matching patients with psychiatric comorbidity to appropriate levels of care.

Summary:

Introduction/Hypothesis: Excessively restrictive placement, according to the American Society of Addiction Medicine's (ASAM) Patient Placement Criteria (PPC-1; 1996), may promote no-shows in psychiatrically comorbid substance abuse patients, because of three hypothetical predictors: female gender, anxiety symptoms, and a supportive social/family environments.

Methods: Treatment seeking adults (N=700), following a computer-assisted ASAM PPC-1 structured interview, were randomly assigned to either Level-of-Care-II (intensive outpatient) or LOC-III (residential treatment). Patients scored as needing LOC-II but assigned to LOC-III were considered "over-matched". Among 143 over-matched patients, no-shows to treatment initiation were significantly higher in comorbids vs. non-comorbids (54% vs. 28%, $P<0.01$).

Results: Among overmatched comorbids who no-showed, there were more females than in the group that showed, 70.4% vs. 29.6%; $p<0.05$. Among the overmatched group, patients with anxiety had more no-shows vs. patients with minimal or no anxiety, 61.5% vs. 27.9%; $p<0.01$. Among overmatched comorbids, patients with supportive social/family/environmental status had more no-shows vs. patients with less supportive social/family/environmental status; 73.3% vs. 25.0%; $p<0.01$.

Conclusions/Discussion: Female gender and having anxiety symptoms appear to undermine the likelihood to show when matched to an overly confining inpatient treatment program. Overmatching may also disrupt the routines of patients who already have stable and structured environments.

Supported by NIDA Grants # R01-DA08781 and K24-DA00427

References:

1. Rubin A: Patient Placement Criteria and Their Relation to Access to Appropriate Level of Care and Engagement in Alcoholism Treatment. In Recent Development in Alcoholism 15: Services Research in the Era of Managed Care, edited by Galanter. Kluwer Academic/Plenum Publishers, New York, 2001.
2. Gastfriend DR: Addiction Treatment Matching: Research Foundations of the American Society of Addiction Medicine (ASAM) Criteria. Binghamton, NY, The Haworth Press, Inc., 2003.

NR157 Monday, May 22, 1:00 PM - 2:30 PM

Rates of PTSD in Service Members Evacuated From Iraq for Battlefield Injury, General Medical Concerns, and Psychiatric Reasons

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Educational Objectives:

At the conclusion of this presentation the participant should have a better understanding of PTSD rates in injured service personel.

Summary:

Background: Post Traumatic Stress Disorder (PTSD) is a risk of war. Hoge et al [1] reported 12.9 % of Service Members met strict criteria for PTSD, and 18% met the broad definition. This report found that being wounded significantly increased the risk of PTSD. Grieger et al [2] found lower rates in Service Members requiring extended hospitalization. We examined the medical records of Service Members medically evacuated from Iraq to investigate rates of PTSD according to reason for evacuation.

Methods: Records were reviewed in 199 Service Members medically evacuated to Naval Medical Center San Diego (NMCSD). Diagnosis of PTSD or Acute Stress Disorder (reported together as PTSD) was identified according to branch of service and reason for evacuation. Results were compared by Chi-square.

Results: 199 Service Members screened. 178 were Marines, 19 were Navy, and 2 were in other branches. 46 Marines (26%), 6 Navy (32%), and 1 other Service Member (50%) had a diagnosis of PTSD at NMCSD. Of the 199, 133 were evacuated for battlefield injuries, 41 for other medical or surgical problems, and 26 for psychiatric reasons. 34 (26%) battlefield injury patients were diagnosed with PTSD, 7 (17%) of the medical patients, and 12 (48%) of the psychiatric evacuees. Chi-square for injury type was 7.649 ($p<0.05$). Chi-square for branch of service did not show significance ($p>0.05$).

Comment: Using clinical diagnosis as an indicator, we found that in individuals medically evacuated from Iraq for general medical reasons, rates of PTSD were similar to those previously reported [1] in deployed service members. We found, however, that rates of PTSD were higher in Service Members who were injured in combat or evacuated for psychiatric reasons. Lower rates previously reported in hospitalized patients [2] could be a result of more stringent definitions of PTSD, different treatments received, or other risk factors.

References:

1. 1) Hoge CW, Castro CA, Messer SC, McGurk D, Cotting DI, Koffman RL. N Engl J Med 2004; 251:13-22.
2. 2) Grieger TA, Cozza S, Engel C, et al. Psychiatric Association Annual Meeting, May 25, 2005, Atlanta GA.

NR158 Monday, May 22, 1:00 PM - 2:30 PM

Substance Misuse and Cognitive Functioning in Early Psychosis: Two-Year Follow-Up

Amanda McCleery, B.S. *Centre for Addiction and Mental Health, First Episode Psychosis Program: PRIME Clinic, PRIME Clinic, CAMH, 252 College St, Toronto, ON, M5T 1R7, Canada*, Jean Addington, Ph.D., Rachel Rabin, B.S., Donald E. Addington, M.D.

Educational Objectives:

Learning Objective: The participant will learn that substance use is common in early psychosis and the impact of substance use on cognition.

Summary:

Background: High comorbidity exists between substance use and psychosis. Since substance use has been shown to negatively impact cognitive functioning in the general population, there is concern about the impact of substance use on already compromised cognitive functioning. However, the literature regarding the effects of substance use on cognition in early psychosis patients is inconclusive. The purpose of this study was to examine the relationship between substance misuse and cognitive functioning in a first episode psychosis sample for two years following admission to a specialized early psychosis program. *Method:* Subjects (n=183; 127 men, 56 women) were assessed at baseline, 12 months (n=183) and 24 months (n=149) using the Case Manager Rating Scale (CMRS) for substance use and a comprehensive cognitive battery. *Results:* At baseline, 49.7% (91) of the sample used substances (alcohol n=25, cannabis n=24, polydrug n=42). At 12 months only 27.4% used substances and 20.8% were using at 24 months. A factor analysis of cognitive data yielded a single cognitive factor. At baseline, the cognitive performance of substance users was significantly better than non-users (F=4.761, p= 0.030). This relationship was not found at 12 and 24 months. *Conclusion:* There was a high incidence of substance misuse in this sample at baseline, which did decrease over the two-year follow-up period. The lack of significant associations between poor cognitive functioning and substance misuse does not support the idea that substance use is negatively impacting cognition. However, the fact that at baseline, when the heaviest use was noted, the users had superior functioning has implications for improved understanding of who might be using substances in the early stages of a psychotic illness.

References:

1. Pencer A, Addington J: Substance use and cognition in early psychosis. J Psychiatr Neurosci 2003; 28: 48-54.
2. Sevy S, Robinson DG, Solloway S, Alvir JM, Woerner MG, Bilder R, Goldman R, Lieberman J, Kane J: Correlates of substance misuse in patients with first-episode schizophrenia and schizoaffective disorder. Acta Psychiatr Scand 2001; 104: 367-374.

NR159 Monday, May 22, 1:00 PM - 2:30 PM

Depression Predicts Mortality in Patients With Kidney Transplants

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Educational Objectives:

Depression is a new strong, significant and independent predictor of mortality and graft failure in kidney transplanted patients.

Summary:

The prevalence of depression has been shown 20-30% in kidney transplanted (Tx) patients. Depression is associated with mortality in patients with several chronic medical conditions, however, it is not known whether depression affects outcomes in Tx patients.

1067 Tx patients were enrolled in a prospective cohort study. Demographic information, medical history, laboratory results and information on medication were collected at enrollment. The patients completed the Center for Epidemiologic Studies-Depression (CES-D) scale which had been validated by our team earlier in Hungarian hemodialysis and Tx patients. Patients have been followed for about 3 years after the baseline visit, and information on death or graft failure (GF) (return to dialysis) was collected.

The initial refusal rate was 20%. The mean age of participants (n=851) was 49+13 years, 59% were males and 17% suffered from diabetes mellitus. 27% of the patients scored 16 or higher on the CES-D questionnaire, suggesting the presence of significant psychological distress. Both the mortality rate and the GF rate of the transplanted kidney were significantly higher in patients with depressive symptoms than in patients without depression (mortality: 15% vs 8%; p=0.003; GF: 11% vs 5%; p=0.004). After controlling for important clinical co-variables in multivariate Cox proportional hazards models, the CES-D score was significantly associated both with mortality (Hazard ratio[HR]$_{\text{for each 1 point increase}}$= 1.029; 95% CI: 1.007-1.051) and also with GF.

Depression is a significant and independent predictor of mortality and graft failure in kidney transplanted patients.

Grants: OTKA TS 040889, OTKA T038409, NKFP 1/002/2001, ETT 218/2003, TeT Foundation (2005/06, MN), Hungarian Eotvos Scholarship (MN).

References:

1. Baines LS, Joseph JT, Jindal RM: Emotional issues after kidney transplantation: a prospective psychotherapeutic study. Clin Transplant 2002; 16: 455-460.
2. Akman B, Özdemir FN, Sezer S, Micozkadioglu H, Haberal M: Depression levels before and after renal transplantation. Transplantation Proceedings 2004; 36: 111-113.

NR160 Monday, May 22, 1:00 PM - 2:30 PM

Comorbidity of PTSD, Physical Health Problems, and Functional Impairment Among Veterans of Operation Iraqi Freedom One Year After Deployment

Artin Terhakopian, M.D. *Walter Reed Army Medical Center, Psychiatry, 12912 Goodhill Road, Silver Spring, MD, 20906*, Charles W. Hoge, M.D., Carl A. Castro, Ph.D., Stephen C. Messer, Ph.D., Charles C. Engel, Jr., M.D.

Educational Objectives:

At the conclusion of this presentation, the participants should have recognition of 1) the symptoms of posttraumatic stress disor-

der (PTSD), 2) its prevalence among veterans of the war in Iraq, 3) the strong connection between combat injury and PTSD and 4) the strong association of PTSD with physical health problems and functional impairment.

Summary:

Background: Recent data have indicated high rates of post-traumatic stress disorder (PTSD) among soldiers returning from combat in Iraq. Studies from prior wars have shown strong associations between combat-related PTSD and physical health problems post-deployment. However, these studies were generally conducted among veterans years after returning from combat. This study is the first to evaluate the association of PTSD with physical symptoms and other health measures in veterans of Operation Iraqi Freedom.

Methods: We studied the members of U.S. combat infantry units using an anonymous survey that was administered to the subjects one year after their return from combat duty in Iraq (n = 2863). The outcomes included PTSD symptoms, self-rated health, sick call visits, missed work-days and physical symptoms evaluated on the basis of standardized self-administered screening instruments.

Results: The percentage of study subjects whose responses met the screening criteria for PTSD was 16.6% (468/2815). PTSD was significantly associated with lower ratings of general health, higher number of sick-call visits, missed workdays, physical symptoms, and high somatic symptom severity. These results remained significant after controlling for being wounded or injured in the combat zone.

Conclusions: The strong association of PTSD with somatic symptoms, lower self-rated health, sick-call visits and missed workdays among veterans of Operation Iraqi Freedom one year after return from combat is important for guiding the delivery of medical resources to address post-deployment medical and psychiatric needs. Clinicians in all medical specialties need to be aware of the strong co-morbidity of physical health problems and PTSD among veterans of the current war in Iraq.

References:

1. Engel CC, Jr., Liu X, McCarthy BD, Miller RF, Ursano R: Relationship of physical symptoms to posttraumatic stress disorder among veterans seeking care for gulf war-related health concerns. Psychosom Med 2000; 62(6):739-45.
2. Hoge CW, Castro CA, Messer SC, McGurk D, Cotting DI, Koffman RL: Combat duty in Iraq and Afghanistan, mental health problems, and barriers to care. N Engl J Med 2004; 351(1):13-22.

NR161 Monday, May 22, 1:00 PM - 2:30 PM

Effect of Parental Psychiatric Comorbidity on the Mental Health Outcomes of Male Offspring at Age 40

Jyotsna Adma, M.D. *University Of Kansas Medical Center, Psychiatry, 3901 Rainbow Blvd, Kansas City, KS, 66160*, Elizabeth C. Penick, Ph.D., Joachim Knop, M.D., Ann Manzardo, Ph.D., William F. Gabrielli, Jr., M.D., Elizabeth J. Nickel, M.A., Per Jensen, M.D.

Educational Objectives:

At the conclusion of this presentation, the participants should be able to recognize the relationship between parental comorbid psychiatric disorders and mental health outcomes of their sons.

Summary:

Objective: To determine the effect of parental psychiatric comorbidity on the 40-year mental health outcomes, especially drinking outcomes, of male offspring,. *Method*: This high-risk study contains 329 males drawn from a Danish Birth Cohort (1959-1961) who have been followed prospectively for 40 years. Two-thirds were biological sons of fathers treated for alcoholism and one-third were sons of fathers never treated for alcoholism. Data sources over the years have included, personal interviews, rating scales, and psychometric tests as well as information extracted from Danish archival records such as The Central Psychiatric Register. At the 40-year follow up, the psychiatric family histories of both parents obtained from the son and from archival sources were reconfigured to reflect parental dyads with (1) No mental illness or substance abuse in either parent. (2) Substance abuse only in either or both parents. (3) Both substance abuse and mental illness in the parental dyad. *Results*: Parental dyads containing both substance abuse and a comorbid mental illness produced the highest rates of substance dependence in the sons: No parental mental illness = 10%; substance abuse only = 22%; both substance abuse and mental illness = 33%. Comorbidity in a parental dyad was also associated with greater psychiatric comorbidity in the son, for example more depression. On multiple measures of psychosocial functioning, sons from comorbid parental dyads reported more stressors and worries, greater social impairment, poorer coping skills and less self-satisfaction than sons from parental dyads with no mental illness or substance abuse only. *Conclusion*: Psychiatric comorbidity in biological parents appears to be passed on to the son. Parental psychiatric comorbidity also seems to adversely influence many other aspects of the sons' lives that result in poorer self-esteem and poorer psychosocial adjustment.

References:

1. Nurnberger JI, Wiegand MS, Bucholz K, O'Connor S, Meyer ET, Reich T, Rice J, Schuckit M, King L, Petti T, Bierut LJ, Hinrichs AL, Kuperman S, Hesselbrock V, Porjesz B. A Family Study of Alcohol Dependence. Arch Gen Psychiatry 2004;61:1246-1256.
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NR162 Monday, May 22, 1:00 PM - 2:30 PM

Diagnosing BPD: Does the Number of Criteria Met Make a Difference?

Anu Asnaani *Rhode Island Hospital, Department of Psychiatry, Box 5369, 75 Waterman St, Providence, RI, 02912*, Mark Zimmerman, M.D., Iwona Chelminski, Ph.D., Diane D. Young, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to describe the severity of Borderline Personality Disorder in relation to comorbidity of Axis I and Axis II disorders, psychosocial measures, and demographic correlates.

Summary:

Objective - Many studies have compared demographic and clinical characteristics of patients with and without borderline personality disorder (BPD), but there is limited knowledge on differences within the population of borderline patients. One potential index of heterogeneity is disorder severity. In the present report from the Rhode Island Methods to Improve Diagnostic Assessment and Services (MIDAS) project we examine whether the severity of borderline personality disorder, as measured by the number of criteria present, is associated with comorbidity of Axis I and Axis II diagnoses, as well as demographic factors and psychosocial functioning. **Methods** - Two thousand three hundred psychiatric outpatients were interviewed with the Structured Clinical Interview for DSM-IV Axis I disorders (SCID) and the Structured

Interview for DSM-IV Personality (SIDP-IV). Approximately ten percent (n = 237) of the patients were diagnosed with BPD and they were divided into 4 groups based on the number of DSM-IV criteria met (5 [n = 89], 6 [n = 70], 7 [n = 46] and 8 or 9 [n = 32]). **Results** - There were no significant differences between the groups in the number of comorbid Axis I or Axis II disorders, rates of specific disorders, social functioning measures, or demographic correlates. **Conclusions** - Sub-typing of borderline patients by the number of criteria met does not provide an explanation for heterogeneity within BPD patients.

References:

1. Rothschild, L., Cleland, C., Haslam, N., & Zimmerman, M: A taxometric study of borderline personality disorder. Journal of Abnormal Psychology 2003; 112:657-666.
2. Tyrer, P: The problem of severity in the classification of personality disorder. Journal of Personality Disorders 2005; 19:309-314.

NR163 Monday, May 22, 1:00 PM - 2:30 PM

Women of Different Ages in Different Countries Used Different Methods to Kill Themselves: Comparison of Sweden, Taiwan and the United States

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Educational Objectives:

1. Women are often viewed as a group with lower suicide risks; however, their risks are not uniform. Age and cultural background determine their risks and suicide methods.
2. In the comparison between Sweden, Taiwan and the US, we found that in Sweden and the US, middle-aged women had the highest suicide rates, in Taiwan however, highest rates were found among elderly women.
3. In Sweden, the most frequently adopted suicide method for females was poisoning by drugs. For women in the US, firearms were the most preferred methods for the young and the elderly, while middle-aged women used poisons more often. In Taiwan, hanging was the most common suicide method adopted by women, except for the 25-44 age group, which chose poisoning over other ways. The most common agents used in suicide poisoning among American and Swedish women were drugs, whereas in Taiwan, pesticides were the most common agents.
4. This international comparison study informs country-specific suicide prevention strategies targeted at women. For the Swedish women, prescription drug control is key; for American females, both prescription drug and firearm sales control should be policy priorities; in Taiwan, precautions should be taken on toxicity and accessibility of pesticides

Summary:

Objective: To make international comparisons of women's suicide methods by age groups in Sweden, Taiwan and the US.

Methods: Age and method-specific suicide death rates among women in year 2000 for Sweden, Taiwan and the US were calculated for international comparisons. The analysis was stratified into four age groups (15-24, 25-44, 45-64 and 65 years and older) and four suicide methods (poisoning by solids/liquids/gases, hanging, firearm, jumping from heights and others). Suicide by poisoning was further divided into 4 different agents (drugs, other gases, pesticides and others).

Results: In Sweden and the US, the highest suicide rates among women occurred in the 45-64 year-old age group (14.6/per 100,000 population and 6.4/per 100,000 population respectively), while in Taiwan, women 65 years and older suffered the highest suicide rates (23.8/per 100,000 population), way above other age groups and other countries. The predominant suicide method adopted by the Swedish women was poisoning (44.5%) and hanging was the most common method used for women in Taiwan (39.9%). In the US, firearms were the most preferred method for the young (15-24 age group) and the elderly (65 years and older) women, which accounted for 34.6% and 39.0% of suicide deaths respectively, while poisoning was more frequently used among the middle aged group (25-44 years old-- 38.3%, 45-64 years old-- 43.9%). In Sweden and the US, drugs were the most common agents used in poisoning suicide among women, while in Taiwan, pesticides were the predominant agents. Male/female suicide ratio also varied between countries, lowest ratio was found in Taiwan (2.11), followed by Sweden (2.39), with the US having the highest (4.39) suicide sex ratio.

Conclusion: Women in different countries of different ages used different methods to commit suicide. The unique features of women's suicidal phenomenon deserve further exploration.

References:

1. Diekstra RFW: Suicide and the attempted suicide: An international perspective. Acta Psychiatr Scand 1989; 80 (suppl): 1-24.
2. Hawton K: Sex and suicide: Gender differences in suicidal behaviour. Br J Psychiatry 2000; 177: 484-485.

NR164 Monday, May 22, 1:00 PM - 2:30 PM

Catatonia in a Hospital Based Predominantly African-American Population

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Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the need for early recognition of catatonia, appropriate treatment and monitoring, prevention of complications, and comprehensive treatment planning.

Summary:

Catatonia is a severe, potentially life-threatening condition associated with psychiatric disorders, yet its prevalence and pathogenesis is not well understood. Higher rates of untreated psychiatric and medical illnesses in the African-American population and greater risk of ExtraPyramidal Symptoms, suggest a higher risk of catatonia in this population. An observation of a dramatic case led to a systematic study of catatonia in our university hospital, which serves a predominantly African-American, socio-economically disadvantaged population. The study objective is to estimate the incidence and characterize the presentation of catatonia in patients seen on the psychiatric inpatient and consultation services of Howard University Hospital.

Methods: We reviewed consecutive cases, from discrete time periods, on the psychiatric inpatient and consultation services, for suspected cases of catatonia. Subsequently, a systematic review of the hospital records was done. The DSM IV criteria were used for diagnosis of catatonia.

Results: 5 % of patients seen on each service were found to have suspected cases of catatonia. Criteria of catatonia were met in14 individuals (3 patients had >1 episode); mutism and immobility were the most common features. Of the cases systematically reviewed to date, 70% were women, 90% were African-American, and the mean age was 34.4 yrs. Majority of the patients were not taking their psychotropic medications during the preceding month. The most common principal diagnosis was schizophre-

nia (80%). Only 20% had current substance abuse which is lower than the overall rate on the services. The majority of cases were treated with benzodiazepines and antipsychotics. Complications included dehydration, loss of weight, UTI, rhabdomyolysis, acute renal failure, and one death due to pulmonary embolism.

Conclusions: Catatonia is not uncommon in our minority population, and appears to be associated with untreated psychiatric illness. Early recognition and treatment appears crucial toward preventing complications.

References:

1. Caroff SN, Mann SC, Francis A, Fricchione GL: Catatonia: From Psychopathology to Neurobiology. Washington, DC, American Psychiatric Publishing, 2004.
2. Rosebush PI, Hildebrand AM, Furlong BG, Mazurek MF: Catatonic syndrome in a general psychiatric inpatient population: frequency, clinical presentation, and response to lorazepam. J Clin Psychiatry 1990; 51:357-362.

NR165 Monday, May 22, 1:00 PM - 2:30 PM

Association of Insight With Psychotic Symptoms, Depression, and Cognition in Early Psychosis: Three-Year Follow-Up

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Educational Objectives:

At the conclusion of this presentation the participant should have a better understanding of insight and its impact on symptoms, cognition and depression over 3 years in a large first episode psychosis population.

Summary:

Background: Recent research has begun to examine the level of insight following a first episode of psychosis since this may have implications for outcomes. *Method:* Insight was investigated in 278 individuals consecutively admitted to a comprehensive early psychosis treatment program. Insight was assessed on admission and after one, two and 3 years. Other measures included PANSS, Calgary Depression Scale for Schizophrenia and a comprehensive cognitive battery. *Results:* Insight improved significantly from a rate of 60% with good insight at baseline to 80% with good insight at 1 year ($t=4.28$, $p<0.001$). Insight remained high at years 2 and 3, but was not significantly better then the level at 1 year ($t=-.62$, $p>0.05$; $t=0.56$, $p>0.05$, respectively). A comparison of those with good to those with poor insight revealed that at each assessment point those with poor insight had significantly higher ratings on positive and negative symptoms and on a general psychopathology scale ($p<0.01$ for each). Those with good insight had significantly higher levels of depression at baseline ($t=3.21$, $p=0.001$). With respect to cognition there were no differences between the 2 groups at any of the assessment times on any of the individual cognitive measures. However using a composite cognitive factor there was a small but significant advantage for the high insight group at one year ($t=2.43$, $p=0.02$). *Conclusion:* A significant proportion of individuals have good insight following a first episode of psychosis. For this group depression may be a significant concern at least upon initial presentation. Those with poor insight have increased symptoms throughout the first three years and possibly poorer cognitive functioning. An improved understanding of insight following a first episode has implications for treatment.

References:

1. Mintz A, Addington J, & Addington D: Insight in Early Psychosis: A One-Year Follow-up. Schizophr Res 2004; 67: 213-17.
2. Crumlish N, Whitty P, Kamali M, Clarke M, Browne S, McTigue O, et al.: Early insight predicts depression and attempted suicide after 4 years in first-episode schizophrenia and schizophreniform disorder. Acta Psychiatr Scand 2005; 112:449-55.

NR166 Monday, May 22, 3:00 PM - 5:00 PM

Algorithm-Guided Treatment of Depression Compared to Treatment as Usual and Genetic Prediction of Response to Lithium Augmentation: The German Algorithm Project (GAPIII)

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Educational Objectives:

At the conclusion of this presentation of the German Algorithm Project (GAP) the participant should be familiar with the principles and effects of algorithm-guided treatment of depression in clinical practice.

Summary:

Treatment algorithms in the clinical care of patients suffering from MDD are considered important instruments in avoiding and overcoming treatment-resistant depression. The multiphasic German Algorithm Project (GAP) has evaluated algorithm-guided treatment of inpatients with MDD. Phase I (observational trial) showed a moderate acceptance but good clinical effectiveness of a standardized stepwise drug treatment regimen (SSTR). Phase II (randomized controlled trial) demonstrated a higher probability of achieving remission for SSTR compared to treatment as usual (TAU).We present the results of the recently finished third phase (GAP III) wich was realized within the German Research Network on Depression. GAP III compared an SSTR and a computerized documentation and expert system (CDES) with TAU in 429 inpatients treated for MDD in a five-arm multicenter randomized controlled trial. Within the SSTR we compared three different second-step strategies in the case of non-response to an initial antidepressant monotherapy (SSTR1: lithium augmentation, SSTR 2: dose escalation of the antidepressant, SSTR 3: switch to other compound). In addition, we searched for an association of the 50-T/C-SNP of the glycogen-synthase-kinase (GSK3-beta) gene with response to lithium augmentation in non-responders to an initial antidepressant monotherapy (n=81).

Preliminary analyses of phase III show a significantly higher hazard ratio (HR) for the time to remission for SSTR (HR: 1.5; p=.01) but not for CDES (HR: 1.06; p=.81) compared to TAU. Patients of older age (>60a) (HR: 5.5; p=.006) and patients with more than one episode (HR: 1.94; p=.004) particularly benefit from SSTR. We identified the c-allele of GSK3-beta to be associated with a superior response to lithium augmentation (HR: 2.3; p=.02) compared to the wildtype (T/T).

Algorithm-guided (i.e. SSTR based) treatment of depression may lead to a shorter time to remission. A genotype-based treatment pathway may represent an approach to optimize and individualize algorihm-guided treatment.

References:

1. Adli M, Rush AJ, Moeller H-J, Bauer M: Algorithms for Optimizing the Treatment of Depression: Making the Right Decision at the Right Time. Pharmacopsychiatry 2003; 36: 222-229.
2. Trivedi MH, Rush AJ, Crismon ML, Kashner TM, Toprac MG, Carmody TJ et al: Clinical results for patients with major depressive disorder in the Texas Medication Algorithm Project. Arch Gen Psychiatry 2004; 61: 669-680.

NR167 Monday, May 22, 3:00 PM - 5:00 PM

Effect of High Dose Venlafaxine XL on QTc and Other Cardiovascular Parameters

Faouzi D. alam, Sr. *Manchester royal infirmary, psychiatry, St Helens, United Kingdom*, Patrick S. Mbaya, Sr., M.D., Sindhu Ashim, Sr., Psy.D., Bennett David, Sr., M.D.

Educational Objectives:

Objectives: To assess the effect of high dose venlafaxine XL on QTc, blood pressure, heart rate and other cardiovascular parameters.

Summary:

Method: The data presented is part of a prospective open label high dose venlafaxine XL study looking at efficacy, serum levels and tolerability undertaken at the Department of Psychiatry, University Hospitals, and South Manchester. Effects of high dose venlafaxine XL (mean 346.15 mg; range 225 mg to 525 mg) on the cardiovascular system in thirty-seven patients with MDD were evaluated. Effects on BP, ECG (PR, QRS, and QTc intervals) and heart rate were studied.

Results: 13.5% of patients were diagnosed with hypertension after starting treatment with venlafaxine. There was an association between heart rate and the dose of venlafaxine although not statistically significant. There was no association between dose of venlafaxine XL and PR, QRS and QTc intervals. One patient on 300 mg who was hypertensive, had other co-morbid physical conditions and was on other medications that may prolong QTc, had mildly prolonged QTc. However this was not clinically significant.

Conclusion: This study with subjects on high dose Venlafaxine (mean 346.15 mg; range 225 mg to 525 mg) did not demonstrate any clinical or statistically significant effects on ECG parameters including PR, QRS Duration and QTc interval.

Keywords: high dose; venlafaxine XL; ECG; cardiovascular effects; QTc.

References:

1. 8. Khawaja IS, Feinstein RE. Cardiovascular effects of selective serotonin reuptake inhibitors and other novel antidepressants. Heart Disease 2003; 5: 153-160.
2. 6. Harrigan RA, Brady WJ. ECG abnormalities in tricyclic antidepressant ingestion. Am J Emerg Med 1999;17:387-393.

NR168 Monday, May 22, 3:00 PM - 5:00 PM

Augmentative Intravenous Clomipramine in Partial Responder Major Depressives: A Single-Blind, Placebo-Controlled Study

Carlo Alfredo Altamura, Prof. Dr. *Dept. of Psychiatry, Department of Clinical Sciences "Luigi Sacco", University of Milan, Italy, Dept. of Psychiatry, Department of Clinical Sciences "Luigi Sacco", University of Milan, Italy, via GB Grassi 74, Milan, 20157, Italy*, Silvia Zanoni, M.D., Monica Bosi, M.D., Emanuela Mundo, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to evaluate the efficacy of low dose intravenous (i.v.) clomipramine augmentation in Major Depressive Episode patients with partial or no response to selective serotonin reuptake inhibitors (SSRIs).

Summary:

Objective: The aim of this study was to evaluate the efficacy of low dose intravenous (i.v.) clomipramine augmentation in Major Depressive Episode patients with partial or no response to SSRIs. *Methods*: 44 patients with DSM-IV TR Major Depressive Episodes and partial (HAM-D total score reduction >25% and <50%) or no response (HAM-D total score reduction <25%) to adequate SSRI treatment were randomized to be treated with i.v. clomipramine (25 mg in 250cc saline) (N=22) or placebo (250 cc saline) (N= 22) as adjunctive treatment for 5 consecutive days. All patients gave their informed consent to participate into the study. HAM-D and MADRS were administered daily by raters blind to the treatment group each patient was assigned to. ANOVA with repeated measures were used on HAM-D and MADRS total scores. In these analyses time and treatment were the independent variables. In addition the number of patients who obtained remission (HAM-D total score <8) was computed and compared between the two treatment groups. *Results*: ANOVA on HAM-D total scores have shown a significat effect of the active treatment (Time x Treatment effect: F=20.940, p=0.0001). The same result was found considering the MADRS total scores (Time x Treatment effect: F=20.716, p=0.0001). Complete remission of symptoms was obtained in 11 patients (50%) treated with clomipramine and in none of the patients treated with placebo. *Conclusions*: Results from this study suggested that low dose i.v. clomipramine can successfully and rapidly treat partial or non responder major depression patients.

References:

1. Suhara T, TakanoA, Sudo Y, et al. High levels of serotonin transporter occupancy with low-dose clomipramine in comparative occupancy study with fluvoxamine using positron emission tomography. Arch Gen Psychiatry 60(4):386-91;2003.
2. Mundo E, Bareggi SR, Altamura AC. Intravenous antidepressants: a pharmacokinetic perspecive on response and resistance in major depression and OCD. Presented at the 156th Annual Meeting of the American Psychiatric Association, San Francisco, CA, May.

NR169 Monday, May 22, 3:00 PM - 5:00 PM

A New Approach for Assessing Patients With GAD or Major Depression and Residual Symptoms

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to assess the value of a new instrument for the identification of residual symptoms in patients with generalized anxiety disorder and major depressive disorder.

Summary:

Background: Two patient-rated Most Troubling Symptoms (MTS) scales were developed and are being used in studies of patients with GAD or MDD with residual symptoms despite adequate therapy.

Methods: Patients with DSM-IV GAD (N=390) and MDD (N= 218) diagnoses and residual symptoms completed an MTS scale. The GAD MTS consists of 7 GAD symptoms and the MDD MTS consists of 8 MDD symptoms; each symptom was patient rated from 0-10 via a telephone Interactive Voice Response System (Healthcare Technology Systems). Patient ratings also included the Quality of Life, Enjoyment and Satisfaction Questionnaire (Q-LES-Q) and the Patient Global Improvement Scale (PGIS). Healthcare professionals rated patients with the HAM-A for anxiety, HAM-D for depression, Clinical Global Impressions of Severity (CGI-S), and Sheehan Disability Scale (SDS). Pearson correlations examined the relationship between the MTS total score and HAM-A, HAM-D, CGI-S, SDS, PGIS, and Q-LES-Q scores.

Results: The 4 MTS items selected most frequently to be the most troubling were excessive anxiety or worry (identified by 76%), feeling restless (68%), trouble sleeping (66%), and getting tired

easily (55%) in the GAD study; and trouble concentrating (70%), sadness (69%), reduced involvement (59%), and feeling tense or uptight (54%) in the MDD study. After a 6-week treatment period, the GAD MTS total score was significantly correlated (P<0.001) with scores on the HAM-A (r=0.65), PGIS (r=0.64), CGI-S (r= 0.58), SDS (r=0.78), and Q-LES-Q (r=-0.72). In patients with MDD, the MTS total score was significantly correlated (P<0.001) with scores on the HAM-D (r=0.67), PGIS (r=0.65), CGI-S (r=0.62), SDS (r=0.80), and the Q-LES-Q (r=-0.76).

Conclusions: The patient-rated MTS tools appear to be useful instruments for assessing residual symptoms in GAD and MDD patients. MTS scores correlated highly with those of well-established clinician- and patient-rated instruments assessing multiple domains.

Supported by Janssen, L.P.

References:

1. Wittchen HU, Zhao S, Kessler RC, et al. DSM-III-R generalized anxiety disorder in the National Comorbidity Survey. Arch Gen Psychiatry 1994;51:355-364.
2. Kessler RC, Berglund P, Demler O, et al. The epidemiology of major depressive disorder: results from the National Comorbidity Survey Replication (NCS-R). JAMA 2003;289:3095-3105.

NR170 Monday, May 22, 3:00 PM - 5:00 PM

Evidence for a Predominant Time Pattern of Drug Use in Bipolar Disorder: Cannabis and Alcohol Precede Affective Symptoms

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Educational Objectives:

At the conclusion of this presentation the participants should know more about time patterns of drug use (alcohol and cannabis) during the course of bipolar disorder. The hypothesis that drug use precedes affective symptoms (and only rarely vice versa) might improve clinical work with the patients because of a hightened understanding of the pattern of this frequent comorbidity. In addition, the hypothesis may prove scientifically fruitful as it could help to explain the interplay of the co-occurrence of bipolar disorder and drug use.

Summary:

Background: A high prevalence of substance use disorder (SUD) comorbidity has been shown for bipolar disorder patients. It is unclear, however, why this particular co-occurrence exceeds SUD comorbidity in many other psychiatric disorders. In part, this is due to the unknown time pattern of drug use and affective episodes.

Methods: We investigated the time pattern of drug use and affective epsiodes in a sample of 166 DSM-IV first episode bipolar-I patients (46% female) from the prospective *Harvard-McLean First Episode Study*. We searched for time patterns of the presence of drug use (cannabis, alcohol) and the presence of affective symptoms (mania, depression; including subthreshold symptoms) during three-months intervals. The observation period was 4.7 years (± 2.6) on average. In a multivariate analysis data were controlled for sex, age, and baseline severity of affective illness (BPRS).

Results: We found a robust association between cannabis use and manic symptoms during the same three months-interval (p<0.001, z: 3.63) and between manic symptoms and cannabis use in the previous three months (p<0.001, z: 3.80). No association was found between manic symptoms and cannabis use in the following interval (p .608, z: 0.51) and also between depressive symptoms and cannabis use during the same, the preceding, or the following interval. There was an association between alcohol use and symptoms of depression during the same three months interval (p=0.028, z: 2.19), and symptoms between depression and alcohol use in the preceding quarter (p=0.007, z: 2.67). In our sample, no association was found regarding alcohol use in the three months interval following an interval with depressed symptoms (p=0.213, z: 2.19) and also between alcohol consumption and manic symptoms.

Conclusions: Drug use might cause affective symptoms rather than being a treatment attempt for affective symptoms. Also, this possible causal relationship might be specific for cannabis (mania) and alcohol (depression).

References:

1. Baethge C, Baldessarini RJ, Khalsa HMK, Hennen J, Salvatore P, Tohen M. Substance Abuse in First-Episode Bipolar I Disorder: Indications for Early Intervention. Am J Psychiatry 2005; 162:1008-1010.
2. Strakowski SM, DelBello MP, Fleck DE, Adler CM, Anthenelli RM, Keck PE Jr., Arnold LM, Amicone J. effects of co-occurring alcohol abuse on the course of bipolar disorder following a first hospitalization for mania. Arch Gen Psychiatry 2005; 62:851-8.

NR171 Monday, May 22, 3:00 PM - 5:00 PM

Suicidal Ideation, Mood Variability, and Religion: A Pilot Study

Marilyn Baetz, M.D. *University of Saskatchewan, Department of Psychiatry, University of Saskatchewan, Ellis Hall, 103 Hospital Drive, Saskatoon, SK, S7N 0W8, Canada*, Rudy C. Bowen, M.D., Anna Nielson, M.S.

Educational Objectives:

At the conclusion of this presentation the participant should be able to discuss mechanisms by which religion/spirituality may relate to mental health. They may also be able to describe the potential relationship between mood variability, religion/spirituality and suicide.

Summary:

Objective: This study investigates the relationship of mood variability and religion/spirituality to suicidal ideation.

Methods: Seventy-four depressed psychiatric patients (42% inpatients, 67% female) completed the MINI interview and self report measures including Beck Suicide Scale, religion/spirituality (Duke Religion Index, Daily Spiritual Experiences, positive and negative religious coping) and mood variability (TempsA cyclothymia) along with the Beck Depression Inventory, Perceived Stress Scale, social support, substance use and demographics. Linear regression was used to determine predictors of suicidal ideation.

Results: All subjects were currently depressed and 80% met criteria for at least one other diagnosis. Mood variability correlated positively with suicidal ideation, and negative religious coping. Mood variability correlated negatively with religion/spirituality measures and positive religious coping. Although the correlations were in the expected direction the relationship only reached significance with a few measures. Measures of suicide correlated negatively and significantly with religion/spirituality and positive religious coping and positively with negative religious coping. Predictors of suicidal ideation in a linear regression model were higher BDI, negative religious coping, lower income and lower worship frequency.

Conclusion: In a general psychiatric population lower religion/spirituality were significantly associated with higher suicidal ideation after controlling for demographic, social support and mood

variability. The small sample size and limited measure of mood variability are a limiting factor.

References:

1. Dervic, K., Oquendo MA, Grunebaum MF, Ellis S, Burke AK, Mann JJ. Religious affiliation and suicide attempt. Am J Psych 161:2303-2308.
2. Witte TK, Fitzpatrick KK, Joiner TE, Schmidt NB. Variability in suicidal ideation: A better predictor of suicide attempts than intensity or duration of ideation? JAD 88:131-126, 2005.

NR172 Monday, May 22, 3:00 PM - 5:00 PM

Chronic Fluoxetine Treatment, Neurogenesis, and Synaptic Plasticity in Rodents and Humans

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Educational Objectives:

1)At the conclusion of this presentation, the participant should be able to understand the use of Transcranial Magnetic Stimulation (TMS) to study cortical plasticity in humans

2)At the conclusion of this presentation, the participant should be able to recognize the neurogenesis-dependent and -independent changes in hippocampal LTP induced by chronic fluoxetine treatment

3)At the conclusion of this presentation, the participant should be able to design pharmacological translational studies by combining TMS and slice physiology

4)At the conclusion of this presentation, the participant should be able to understand the effects of chronic fluoxetine treatment in motor, cognitive and mood related brain areas

Summary:

Introduction/Hypothesis

During the last few years several studies have highlighted the possibility that mood disorders can be characterized by changes in brain plasticity. We investigated the hypothesis that chronic administration of fluoxetine might affect long-term potentiation (LTP), an important model of neuronal plasticity in rodents and humans.

Methods

We studied associative LTP-like plasticity in primary motor cortex (M1) with paired associative stimulation (PAS-Transcranial magnetic stimulation combined with sensory stimulation) in a randomized, double-blind, crossover study. Ten right-handed normal subjects received 20 mg daily of either fluoxetine or placebo over a period of 30 days with a 3 month washout. LTP was studied in brain slices obtained from chronic fluoxetine- and vehicle-treated mice (fluoxetine, 10mg/kg/day for 4 weeks). LTP was induced in hippocampus Dentate Gyrus (DG) with a neurogenesis-dependent and independent protocol, in the Shaffer Collateral- CA1 pathway, in prefrontal cortex and motor cortex with field potentials technique.

Results

In humans, fluoxetine treatment induced a decrease of M1 PAS-induced associative plasticity accompanied by an increased steepness of the input-output curve.

In rodents, fluoxetine induced an increase in neurogenesis-dependent LTP in DG, an increase in steepness of the input-output curve and a decreased amount of neurogenesis-independent LTP in all tested areas.

Conclusions/Discussion

Chronic fluoxetine treatment induces a saturation of LTP in non-neurogenic areas while increases the number of newly generated neurons in DG and a form of LTP that relies upon their synaptic activity. Multiple factors may contribute to depression by impairing neuronal plasticity and disturbing neurochemical functioning in mood regulatory brain regions. In this study we demonstrated that chronic fluoxetine treatment affects activity-dependent neuroplasticity in rodents and humans. These findings could be relevant for the understanding of the mechanism of action of antidepressant. Furthermore, this experimental approach might represent a novel method for translational pharmacological research in psychiatry.

NR173 Monday, May 22, 3:00 PM - 5:00 PM

Subjective Complaints Versus. Objective Measures of Cognitive Deficits in Minimally Ill Bipolar Disorder Patients

Amber D. Bauer, M.A. *Northwestern University Feinburg School of Medicine, 707 W. Sheridan Rd., Apt. 526, Chicago, IL, 60613,* William S. Gilmer, M.D., Robert Hanlon, Ph.D., Robert T. Dunn, M.D., Jenelle Fleck, M.S.N., S. Nassir Ghaemi, M.D.

Educational Objectives:

To explore discordance between baseline subjective cognitive complaints and baseline objective measures of cognitive performance in minimally ill bipolar patients enrolled in a cognition treatment study. At the conclusion of this poster session, the participant will better understand the discordant association between subjective complaints and objective cognitive performance on measures of verbal and non-verbal learning and memory, attention, and executive functioning.

Summary:

Background: Complaints of cognitive impairment are common in patients with bipolar disorder [1]. Impairments in executive functioning, attention, visual-spatial abilities, memory, and verbal fluency have been shown on objective measures during acute and euthymic states [2]. Understanding the relationship of subjective complaints and objective cognitive performance is essential to designing studies of appropriate therapeutic interventions. Such interventions are lacking to date. The aim of this analysis was to explore concordance between subjective cognitive complaints and objective performance in minimally ill bipolar patients.

Method: As part of an intervention study for bipolar patients with baseline reports of cognitive impairment, minimally ill bipolar outpatients were recruited and administered a clinical neuropsychological battery assessing estimated premorbid IQ, attention, verbal and non-verbal learning and memory, and executive functioning.

Results: In an interim analysis, 7 of 10 patients reported subjective cognitive complaints, despite objective measures of cognitive performance at or above normal limits. Test scores will be reported and patterns of impairment will be analyzed on an entire sample of 30 patients. Incidence of discordance between subjective complaints and objective impairment will be reported. Secondary analyses will be conducted to detect association of demographic and illness related variables on objective performance.

Conclusions: While varied patterns of neurocognitive impairment occur in minimally ill bipolar patients, preliminary observations demonstrate inconsistencies in subjective reports and objective performance. Such inconsistencies may complicate studies aimed to identify treatment strategies to treat cognitive dysfunction in bipolar patients. Explanations for these inconsistencies will be proposed. In addition to enrollment criteria based upon demonstrated objective impairment at baseline, we recommend that future cognitive treatment studies include symptom validity tests, as well as measures of neuroticism and attributional style.

References:

1. Murphy, FC, Sahakian, BJ. Neuropsychology of bipolar disorder. British Journal of Psychiatry'Supplement 2001; 41: s120-7.

2. Sweeney, JA, Kmiec, JA, Kupfer, DJ. Neuropsychological impairments in bipolar and unipolar mood disorder on the CANTAB neurocognitive battery. Society of Biological Psychiatry 2000; 48: 674-85.

NR174 Monday, May 22, 3:00 PM - 5:00 PM

Self-Reported Days of Hypomania Outside Episodes and Minimum Episode Length

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Educational Objectives:

The viewer should understand the relationship between the duration requirement for an episode of hypomania and both the number of episodes and number of patients that will meet the criteria.

Summary:

Objective: To investigate the relationship between the minimum length for an episode of hypomania, and the number of episodes and days of hypomania outside of episodes.

Method: 203 patients (135 bipolar I; 68 bipolar II) recorded mood daily (30,348 total days; mean 149 days) using ChronoRecord computer software. Episodes of hypomania and days of hypomania outside of episodes were determined.

Results: With a minimum hypomania episode length of 4 days as in the DSM-IV, 44 patients experienced 129 episodes, and hypomania was reported on 6.7% of all days outside of episodes (1675 days). Bipolar I patients were more likely to report hypomania outside of episodes (p=.010). With a minimum length of 3 days, 74 patients reported 226 episodes and hypomania was reported on 5.6% of all days outside of episodes (1383 days). With a minimum length of 2 days, 96 patients reported 404 episodes, and hypomania was reported on 4.3% of all days outside of episodes (1017 days). With a length of 2 or 3 days, there was no significant difference in the distribution of hypomania outside of episodes by diagnosis.

Conclusion: As the minimum length for an episode of hypomania decreases, both the number of episodes and the number of patients with episodes increases. Below 4 days, the number of self-reported days of hypomania outside of episodes did not vary by diagnosis of bipolar I or II.

References:

1. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition Text Revision (DSM-IV TR), Ameican Psychiatric Press, Washington, DC 2000.

2. Akiskal HS, Benazzi F. Optimizing the detection of bipolar II disorder in outpatient private practice: toward a systematization of clinical diagnostic wisdom. J Clin Psychiatry. 2005;66:914-21.

NR175 Monday, May 22, 3:00 PM - 5:00 PM

Bipolar Affective Disorders: Activity of the Limbic Hypothalamo Pituitary Adrenal Axis in an Acoustic Startle Paradigm

Serge Beaulieu, M.D. *Douglas Hosp Research Ctr, Bipolar Disorder Program, 6875 LaSalle Blvd, Verdun, PQ, H4H 1R3, Canada*, Trino Baptista, M.D., Mario Roy, M.D., Rebecca Sablé, M.Psy., Joseph Thavundayil, M.D., Ellen Paquet, B.S.N., Sybille Saury, M.Psy.

Educational Objectives:

The aim of this poster is to increase our understanding of the link between the bipolar affective disorders and the activity of the Limbic-Hypothalamo-Pituitary-Adrenal axis.

Summary:

An abnormal stress regulation by LHPA axis could be associated to bipolar affective illness. The aim of our study is to determine if patients with bipolar affective disorder have an increased stress responses than normal control participants. We have measured startle responses in a bipolar disorders group compared with normal volunteers. We have measured physiological responses to 106 db pulse, pre pulse inhibitions (80 or 90 db pulse occuring 60 ms before a 106 db pulse) and startle responses to a fear-potentiated stimulus. In addition, we have correlated baseline plasma cortisol level at study entry (8:00AM) with stress responses and some psychiatric scales (HAMD-21, MADRS, YMRS) . Ours results demonstrate that bipolar patients have a higher blood cortisol baseline level than control participants and the blood cortisol concentration is positively correlated with the intensity of the response to acoustic startle and with HAMD and MADRS scores. Bipolar patients have significantly higher responses than control participants in several conditions including pre pulse inhibition and fear-potentiated startle responses. These results are interpreted in relation with the LHPA hyperactivity observed in some animal model of depression.

References:

1. Daban C, Vieta E, Mackin P, Young AH: Hypothalamic-Pituitary-Adrenal Axis and Bipolar Disorder. Psychiatr Clin N Am 2005; 28: 469-480.

2. Cadenhead KS, Carasso BS, Swerdlow NR, Geyer MA, Braff DL: Prepulse Inhibition and Habituation of the Startle Response are Stable Neurological Measures in a Normal Male Population. Biol Psychiatry 1999; 45: 360-364.

NR176 Monday, May 22, 3:00 PM - 5:00 PM

Metabolic Abnormalities in a Bipolar Subgroup of the Canadian Bipolar Consortium: A Two-Year, Follow-Up Study

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Educational Objectives:

The purpose of this poster is to underline the importance of metabolic abnormalities in the bipolar affective population

Summary:

There is an increase evidence that bipolar patients are more sensitive to several metabolic abnormalities than the rest of the population. We have recorded several type of metabolic data every three months of bipolar patients in several centers across Canada during two years and compiled the results. We present here the analysis of the data from two of these centers. For the first follow up visit, only 24.6% of our bipolar patients (n = 64) have a normal Body Mass Index (BMI<25), 36.2% are overweight and 39.1% are obese (BMI>30), this ratio doesn't significantly change during this two years follow up. The mean blood pressure is 79.8/127.9 (n = 45), mean HDL is 1.10 mmol/L (n = 40), mean Glucose fasting is 5.49 mmol/L (n = 42), mean triglyceride is elevated at 1.92 mmol/L (n = 43). All these metabolic data didn't significantly change during this two years follow up. For these five kind of data the mean metabolic abnormalities is 1.16 per patient per visit for the first year of follow up and, once again, this mean didn't significantly

change during this two years survey. Near 25% of our bipolar patients have at least 3 metabolic abnormalities at each visit during the first year of follow up. These data are showing us the importance for the physician to monitor patient physical health as well as mental health and to create a strategy to reduce these metabolic abnormalities.

References:

1. Baptista T, Kin NM, Beaulieu S, Baptista EA: Obesity and Related Abnormalities During Antipsychotic Drug Administration: Mechanisms, Management and Research Perspectives. Pharmacopsychiatry 2002; 35: 205-219.
2. Baptista T, De Mendoza S, Beaulieu S, Bermùdez A, Martinez M: Metabolic Syndrome during Atypical Anti-Psychotic Drug Treatment: Mechanisms and Management. Metabolic Syndrome and Related Disorders 2005; 2: 290-307.

NR177 Monday, May 22, 3:00 PM - 5:00 PM

Mixed Depression and the Mood Spectrum

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand that there may be a continuity between bipolar disorders and depressive disorders, supporting a spectrum concept of mood disorders, beyond the current categorical split of mood disorders in bipolar disorders and depressive disorders.

Summary:

Background: Mixed states, i.e., opposite polarity symptoms in the same mood episode, question the current categorical split of mood disorders in bipolar disorders and depressive disorders, and support a continuity between mania/hypomania and depression. **Study aim** was to assess the distribution of the hypomanic symptoms present during depression in bipolar II disorder (BP-II) and MDD. A bi-modal distribution would support a categorical distinction, no bi-modality would support a continuity. It was also tested if there were a dose-response relationship between co-occurring hypomanic symptoms and bipolar family history loading, which, if present, would support a continuity.

Methods: Consecutive 389 BP-II and 261 MDD major depressive episode (MDE) outpatients were interviewed (off psychoactive drugs) with the Structured Clinical Interview for DSM-IV, the Hypomania Interview Guide (to assess co-occurring hypomanic symptoms), and the Family History Screen, by a senior mood specialist psychiatrist in a private practice. The distribution of co-occurring hypomanic symptoms in depression in the entire sample was studied by Kernel density estimate and by the histogram method.

Results: As expected, BP-II versus MDD had significantly more co-occurring hypomanic symptoms in depression: irritable mood, talkativeness, racing/crowded thoughts, distractibility, psychomotor agitation, increased goal-directed activity, and excessive involvement in pleasurable activities. Instead, Kernel density estimate distribution, and the histogram of co-occurring hypomanic symptoms, had an almost perfect normal-like shape. The likelihood ratios of different cut points of co-occurring hypomanic symptoms in depression for bipolar family history loading showed a dose-response relationship.

Conclusions: By following the bi-modality approach instead of classic diagnostic validators (such as family history and age at onset), a continuity between BP-II and MDD would seem to be supported. A continuity between BP-II and MDD would also seem to be supported by the dose-response relationship between co-occurring hypomanic symptoms and bipolar family history loading.

References:

1. Benazzi F: Mixed states in bipolar II disorder: should full hypomania always be required? Psychiatry Res 2004;127:247-257.
2. Benazzi F: Mixed depression: a clinical marker of bipolar-II disorder. Prog Neuropsychopharmacol Biol Psychiatry 2005;29:267-274.

NR178 Monday, May 22, 3:00 PM - 5:00 PM

Is Overactivity the Core Feature of Hypomania?

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand that the core feature of hypomania is more likely to be overactivity than mood change (elevated/irritable mood).

Summary:

Overactivity may be as important as mood change (elevated/irritable mood) for the diagnosis of hypomania. **Study aim** was testing this hypothesis. **Sampling and Methods:** Consecutive 137 bipolar II disorder (BP-II) and 76 MDD remitted outpatients were interviewed with Structured Clinical Interview for DSM-IV by a senior clinical research psychiatrist in private practice. Patients were asked if had had hypomanic symptoms and episodes, and which were the most common hypomanic symptoms during various episodes. Study aim had not been planned when variables were collected for different study goals. **Results:** Overactivity was the most common hypomanic symptom in BP-II, and had the strongest association with BP-II among all the hypomanic symptoms (overactivity OR = 15.4, elevated mood OR = 12.6). Three factors were found: "elevated mood" factor including elevated mood and increased self-esteem; "mental activation" factor including racing/crowded thoughts; "behavioral activation" factor including overactivity. There was no relationship between overactivity and mood change. Irritable mood was not associated with overactivity and elevated mood. BP-II was present in 21.6% of patients without history of overactivity, and in 81.0% of patients with history of overactivity. BP-II was present in 25.0% of patients without elevated mood, and in 63.3% of patients with elevated mood. As predictor of BP-II, overactivity had sensitivity = 90.5%, specificity = 61.8%, positive predictive value = 81.0% (elevated mood had 72.2%, 82.8%, and 88.3%, respectively). Five or more hypomanic symptoms had the most balanced combination of sensitivity (82.4%) and specificity (85.5%) for BP-II, and positive predictive value = 91.1%. Overactivity was present in 89.5% of patients with history of >=5 hypomanic symptoms, elevated mood was present in 76.6%. **Conclusions:** Results seem to support the view that overactivity may be a core feature of hypomania, suggesting upgrading of overactivity to a stem criterion for hypomania.

References:

1. Benazzi F: Factor structure of recalled DSM-IV hypomanic symptoms of bipolar II disorder. Compr Psychiatry 2004;45:441-446.
2. Benazzi F, Akiskal HS: The dual factor structure of self-rated MDQ hypomania: energized-activity versus irritable-thought racing. J Affect Disord 2003;73:59-64.

NR179 Monday, May 22, 3:00 PM - 5:00 PM

Mixed Depression and Anxiety Relationship

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand the relationship between mixed depression and anxiety.

Summary:

Background: Recent studies have shown that mixed depression (DMX), i.e., a major depressive episode (MDE) and manic/hypomanic symptoms combined, is prevalent in bipolar disorders, and not uncommon in depressive disorders. The bipolar nature of DMX was supported by its close link to bipolar family history. However, there is an overlap between some DMX symptoms and some anxiety symptoms, suggesting that DMX could be related also to anxiety. Study aim was to test if anxiety symptoms were more severe in bipolar-II disorder (BP-II) versus MDD. As DMX was found to be more common in BP-II versus MDD, if there were a relationship between DMX and anxiety, than anxiety symptoms should be more severe in BP-II versus MDD. **Methods:** Consecutive 557 MDE outpatients (251 BP-II, 306 MDD) were interviewed with the Structured Clinical Interview for DSM-IV, and the Montgomery and Asberg Depression Rating Scale (MADRS), by a senior clinical and research psychiatrist in a private practice. The study sample was collected before our start of the studies on DMX, thus avoiding any possible bias. MADRS items related to anxiety symptoms are inner tension, reduced sleep, concentration difficulties, and lassitude. **Results:** By one-way analysis of variance controlled for age and gender, and by the nonparametric Kruskal-Wallis test, there were no significant differences on MADRS items severity between BP-II and MDD. **Conclusions:** Findings do not seem to support a relationship between DMX and some anxiety symptoms, as, if there were such a relationship, anxiety symptoms should have been more severe in BP-II versus MDD (as DMX is more common in BP-II, and some DMX and anxiety symptoms overlap). Findings may be important for depression treatment, as the bipolar nature of DMX would suggest using more mood stabilising agents than antianxiety agents.

References:

1. Benazzi F: Family history validation of a definition of mixed depression. Compr Psychiatry 2005;46:159-166.
2. Bauer MS, Simon GE, Ludman E, Unutzer J: ƒBipolarity§ in bipolar disorder: distribution of manic and depressive symptoms in a treated population. Br J Psychiatry 2005;187:87-88.

NR180 Monday, May 22, 3:00 PM - 5:00 PM

Complexity of Depression Treatments: Healthcare Utilization and Costs

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that patients with difficult-to-treat depressive disorders are not optimally treated and have higher resource utilization and costs.

Summary:

Introduction: Depressive disorders are debilitating with significant economic consequences [1]. Patients with difficult-to-treat depressive disorders not optimally treated with initial regimens have higher resource utilization and costs [2]. This study investigated treatment patterns and one-year costs for patients based on degree of treatment complexity.

Methods: Study population included patients 18 years old or greater with depressive disorders (n = 71,731) from a national managed-care claims database. Patients were stratified into five treatment groups (untreated, mono-therapy, second-line, third-line and advanced therapy) based on treatment complexity. Classifications were determined by medication use (anti-depressants, mood stabilizers and anti-psychotics) and patterns of switching and titration. Demographics (age, gender), physician specialty and annual healthcare costs for 2003 (total and depression-related), were determined for the population and each of the treatment groups.

Results: Patients were classified as follows: 42.2% untreated, 38.2% mono-therapy, 15.9% second-line, 0.6% third-line and 3.1% advanced therapy. Annual health costs for the population increased substantially by degree of complexity, from $4,706 for the untreated group to $18,516 for the advanced therapy group. The proportion of depression-related costs increased from 15.4% for the untreated group to 45.8% for the advanced therapy group.

Conclusions: The substantial use of multiple drugs and frequency of switching and titration in depression treatment indicates that there is still unmet need for new therapies. Finding treatments that achieve optimal benefits with less switching and titration and fewer medications will have substantial economic benefits to the healthcare system.

References:

1. Greenberg, P., et al.: The economic burden of depression in the United States: How did it change between 1990 and 2000? J Clin Psych, 2003. 64: p. 1465-1475.
2. Corey-Lisle, P., et al.: Identification of a claims data "signature" and economic consequences for treatment-resistent depression. J Clin Psych, 2002. 63(8): p. 717-726.

NR181 Monday, May 22, 3:00 PM - 5:00 PM

The Value of Routine Laboratory Monitoring in a Bipolar Specialty Clinic

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Educational Objectives:

At the conclusion of this presentation, the participant will have an understanding of the outcome of an effort to implement recommended guidelines for monitoring of vital signs, EKG, and laboratory work in the care of bipolar patients.

Summary:

Objective: To examine the outcome of recommended clinic guidelines in a bipolar specialty clinic, monitoring vital signs, EKG, and laboratory work related to medication monitoring and concerns related to cardiac and metabolic abnormalities.

Method: We reviewed the charts of 257 patients who had a clinic visit between January 1 and March 31 of 2005. 121 (47%) of the charts recorded vital signs, EKG, and laboratory tests. The treating clinician recorded if the results were clinically significant. Review of all clinically significant results were further classified as new findings or previously known abnormalities.

Results: Of the 121 subjects, 69 (57%) had one or more lab results outside of reference range but only 24 (9.3%) had clinically significant abnormalities. 5.6% of 88 glucose levels, 5.7% of 87 TSH levels, 1.3% of 78 BUN levels, 2.3% of 88 creatinine levels, 1.3% of 80 WBC levels, 5.4% of 55 electrolyte levels, 3.4% of 29 EKGs, and 9.4% of 74 blood levels of lithium, valproic acid, and carbamazepine were found clinically significant.

Conclusions: Routine monitoring detected a modest rate of new clinically meaningful abnormalities.

References:

1. American Psychiatric Association: Practice guideline for the treatment of patients with bipolar disorder (revision). Am J Psychiatry 2002; 159:1-50.
2. Barrett E, Blonde L, Clement S, et al.: Consensus development conference on antipsychotic drugs and obesity and diabetes. Diabetes Care 2004; 27:596-601.

NR182 Monday, May 22, 3:00 PM - 5:00 PM

Treatment Effect in a Severely Depressed Subset of a Placebo-Controlled Trial of Escitalopram and Citalopram

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to gain an understanding of how an elevated placebo response may contribute to the failure of antidepressant trials and understand the role of escitalopram in the treatment of severely depressed patients.

Summary:

Introduction: Severely depressed patients typically respond poorly to placebo and favorably to antidepressants. A placebo-controlled trial of escitalopram and citalopram, which had a high placebo response, was analyzed to determine the treatment effect in severely depressed patients.

Methods: Patients with moderate-to-severe MDD (baseline MADRS≥22) were randomized to 8 weeks of double-blind flexible-dose treatment with escitalopram (10-20 mg/day; N=125), citalopram (20-40 mg/day; N=123) or placebo (N=127).

Results: Mean MADRS scores at baseline were 28.7, 28.3, and 28.8, respectively. A total of 43% of placebo completers were responders (50% decrease from baseline MADRS score). At week 8, neither active treatment produced significantly greater mean changes from baseline versus each other or placebo in MADRS total scores (primary efficacy outcome, LOCF); the result was significant for both groups versus placebo in the OC analysis. In severely depressed patients (baseline MADRS score ≥30), escitalopram was superior to both placebo (LSMD [95% CI] -5.67 [-10.4, -0.92], *P*=0.020; LOCF) and citalopram (-5.48 [-10.5, -0.49], *P*=0.032; LOCF). Citalopram treatment was not significantly different from placebo.

Conclusion: An elevated placebo response may contribute to the failure of some antidepressant trials. Escitalopram appears to be more effective than citalopram in treating severe depression.

References:

1. Gorman JM, Korotzer A, Su G. (2002) Efficacy comparison of escitalopram and citalopram in the treatment of major depressive disorder: pooled analysis of placebo-controlled trials. CNS Spectrums 7(suppl 1): 40-44.
2. Owens MJ, Rosenbaum JF. (2002) Escitalopram: a second generation SSRI. CNS Spectrums 7(suppl 1):34-39.

NR183 Monday, May 22, 3:00 PM - 5:00 PM

Escitalopram in the Treatment of PMDD

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Educational Objectives:

The participant will be able to evaluate the efficaciousness of escitalopram in the treatment of premenstrual dysphoric disorder.

Summary:

Introduction: PMDD is a chronic disease occurring in 3-8% of menstruating women (1,2). The current study was designed to evaluate the efficacy and tolerability of intermittent dosing (luteal phase only) with 10 and 20mg escitalopram.

Methods: A total of 158 patients with a diagnosis of PMDD, confirmed during two cycles of prospective self-rating of their symptoms (baseline), were treated for 3 cycles in this single-centre, randomised, double-blind, placebo-controlled 3-arm fixed dose study. The primary measure of efficacy was the relative median change from baseline in the mean of the luteal VAS rating (0-100 mm) for irritability, tension, affective lability, and depressed mood.

Results: The patients had a baseline severity of approximately 50 mm in the mean luteal VAS key psychological symptom score. At endpoint, both escitalopram treatment groups showed superior improvements on the relative median change in the key psychological symptom score *versus* the placebo group [86% decrease for the 10mg escitalopram group ($p<0.01$) and 94% decrease for the 20mg escitalopram group ($p<0.001$) *versus* 69% decrease for the placebo group], with escitalopram 20mg being more efficacious than 10mg ($p<0.01$). Escitalopram reached its maximal effect in the first treatment cycle, and this effect was maintained during the following treatment cycles. The reduction of the key symptom of PMDD, irritability, was 86% (escitalopram 10mg, $p<0.01$), 92% (escitalopram 20mg, $p<0.001$), and 56% (placebo). The percentage of subjects achieving remission (≥80% reduction in the irritability score) was 30% (placebo), 60% (escitalopram 10mg) and 80% (escitalopram 20mg). The most frequent adverse event was nausea. Adaptation of patients to nausea from one treatment cycle to another was marked. The withdrawal rates due to adverse events were 6% (placebo), 13% (escitalopram 10mg) and 6% (escitalopram 20mg).**Conclusions**: Intermittent treatment with escitalopram 10 and 20mg/day was effective and well tolerated in the treatment of PMDD.

References:

1. Angst J., Sellaro R., Merikangas K.R., Endicott J. The epidemiology of perimenstrual psychological symptoms. Acta Psychiatr. Scand. 2001; 104: 110-6.
2. Wittchen H.-U., Becker E., Lieb R., Krause P. Prevalence, incidence and stability of premenstrual dysphoric disorder in the community. Psychol Med 2002;32: 119-32.

NR184 Monday, May 22, 3:00 PM - 5:00 PM

An Epidemiological Survey of Patients Presenting With Dfficult Depression at Private Psychiatric Clinics Throughout France

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Educational Objectives:

This poster gives the reader an appreciation for the variety of symptoms associated with a major depressive episode and the complexity of correctly diagnosing patients with so-called 'difficult depression'.

Summary:

Objective: French patients presenting at private psychiatric clinics with 'difficult depression' were characterized according to depressive disorders and co-morbidities. Management and care

of patients was documented and factors leading to functional handicap evaluated.

Methods: Adult patients showing symptoms of depressive disorders, who had taken antidepressant monotherapy for at least 6 weeks but with insufficient response to treatment, and who were not hospitalized were examined.

Results: In total, 855 patients (67.2% female; mean age 45.1±12.4 years) were examined by 304 investigators (8 months). Most patients had a medical history of mood disorders (83.6%) and were currently suffering a major depressive episode (93.5%). Dysthymia was diagnosed by investigators in 24.6% of patients compared with 58.0% using DSM-IV (M.I.N.I.). Major depressive episodes were unipolar (78.5%), mixed bipolar (6.4%), or non-mixed bipolar (15.1%). Concurrent psychotic symptoms (18.3%), anxiety disorders (93.0%) and personality disorders (62.3%) associated with mood disorders were diagnosed using M.I.N.I. The Sheehan Disability Scale (SDS) identified factors linked to professional, social and domestic handicap. These handicaps were positively correlated ($p<0.05$) with a major depressive episode and history of suicidal behaviour or psychiatric hospitalization.

Conclusion: 'Difficult depression' requires a careful diagnosis in order to ensure that patients with this condition receive optimal treatment.

References:

1. APA. DSM IV, Diagnostic & Statistical Manual of Mental Disorders. 4 ed. Washington D.C.: American Psychiatric Association; 1994.
2. Sheehan DV, et al. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. J Clin Psychiatry 1998;59 Suppl 20:22-33;quiz 34-57.

NR185 Monday, May 22, 3:00 PM - 5:00 PM

Comparative Efficacy of Long-Term Treatment With Escitalopram and Paroxetine in Severe Major Depression

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Educational Objectives:

The participant will obtain knowledge concerning the efficaciousness of escitalopram and paroxetine in the treatment of major depressive disorder.

Summary:

Objective: Escitalopram and paroxetine show efficacy in the treatment of patients with social anxiety disorder (1) and generalised anxiety disorder (2). This randomised, double blind, fixed-dose study evaluated the efficacy of escitalopram and paroxetine in the long-term treatment of patients with severe MDD.

Methods: Patients with DSM-IV-defined MDD and baseline MADRS ≥30, with or without comorbid anxiety, were randomised in a 1:1 ratio to 24 weeks of double-blind treatment with fixed doses of either escitalopram (20 mg) or paroxetine (40 mg). The primary analysis of efficacy was an analysis of covariance (ANCOVA) of change from baseline to Week 24 in MADRS total score (LOCF).

Results: At endpoint (24 weeks), the mean change from baseline in total MADRS score was -25.2 for patients treated with escitalopram (n=228) and -23.1 for patients with paroxetine (n= 223), a difference of 2.1 points ($p<0.05$). The difference on the MADRS (LOCF) was significantly in favour of escitalopram from Week 8 onwards. The proportion of responders (≥50% decrease in MADRS) after 24 weeks was 82% (escitalopram) and 77% (paroxetine). The corresponding values for remission (MADRS ≤12) were 75% (escitalopram) and 67% (paroxetine) ($p<0.05$). The results on the primary efficacy scale were confirmed by significantly greater difference in favour of escitalopram on the HAMA, HAMD, CGI-S, and CGI-I scales. For very severely depressed patients (baseline MADRS ≥35), there was a difference of 3.5 points in favour of escitalopram ($p<0.05$). The overall withdrawal rate for patients treated with escitalopram (19%) was significantly lower than with paroxetine (32%) ($p<0.01$). The withdrawal rate due to adverse events (AEs) was significantly lower for escitalopram (8%) compared to paroxetine (16%) ($p<0.05$). There were no significant differences in the incidences of AEs.**Conclusion**: Escitalopram was significantly more effective than paroxetine in the treatment of patients with severe MDD.

References:

1. Montgomery SA, Nil R, Durr-Pal N, Loft H, Boulenger JP. A 24-week randomized, double-blind, placebo-controlled study of escitalopram for the prevention of generalized social anxiety disorder. J Clin Psychiatry. 2005;66:1270-1278.
2. Baldwin DS, Huusom AKT, Maehlum E. Escitalopram and paroxetine compared to placebo in the treatment of generalised anxiety disorder (GAD). Eur Neuropsychopharm 2004;14(Suppl 3):S311-S312.

NR186 Monday, May 22, 3:00 PM - 5:00 PM

Divalproex Sodium, Extended-Release Versus Placebo in the Treatment of Acute Mania

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Educational Objectives:

Evaluate the safety and efficacy of divalproex extended-release (ER) for the treatment of adult bipolar I disorder, manic or mixed type.

Summary:

Objective: Evaluate the safety and efficacy of divalproex extended-release (ER) for the treatment of adult bipolar I disorder, manic or mixed type.

Methods: A 21-day, randomized, placebo-controlled, parallel-group study was conducted in adult patients hospitalized for acute mania associated with bipolar I disorder. Divalproex Extended Release dosing was initiated at 25 mg/kg/day QD, increased by 500 mg on Day 3, and adjusted to a target serum valproate level of 85-125 mcg/mL. Efficacy assessments included the Mania Rating Scale (MRS; primary endpoint), and percentage of patients meeting criteria for response (>50% improvement on the MRS).

Results: Intent-to-treat efficacy analyses included 364 patients (187 divalproex Extended Release ; 177 placebo). The rapid dose titration designed to achieve therapeutic serum concentrations early in treatment yielded a mean serum valproate level of 96.5 mcg/mL on Day 5 with a mean divalproex Extended Release dose of 2875 mg. Divalproex Extended Release produced superior improvements in manic symptoms versus placebo assessed by the MRS, and more divalproex Extended Release patients met responder criteria versus placebo (all $p < 0.05$). More adverse events were reported in the divalproex Extended Release group versus placebo.

Conclusion: Divalproex Extended Release is a safe and effective treatment for bipolar I disorder, manic or mixed type.

References:

1. Bowden CL et al: Efficacy of divalproex vs lithium and placebo in the treatment of acute mania. JAMA 1993; 54:305-308.
2. Dutta S et al: Comparison of the bioavailability of unequal doses of divalproex sodium extended-release formulation relative to the delayed-release formulation in healthy volunteers. Epilepsy Res 2002; 49:1-10.

NR187 Monday, May 22, 3:00 PM - 5:00 PM

Durability of Antidepressant Response to Vagus Nerve Stimulation

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to discuss the durability of benefits of VNS for treatment-resistant depression.

Summary:

Objective: Vagus nerve stimulation (VNS) has shown efficacy in treatment-resistant depression (TRD). This study characterized the durability of improvement in patients who responded early or late while receiving VNS.

Methods: In both a pilot and pivotal study, patients were identified who had at least a 50% reduction in symptom scores 3 months (early responders) or 12 months (late responders) after starting VNS. Probabilities were determined for maintenance of response at 12-month (early responders) and 24-month (early and late responders) time points. Consistency of symptomatic improvement throughout the 24-month study periods was also evaluated, testing for change in serial depression ratings. The potential confound of alternations in antidepressant treatment was examined in the pivotal trial.

Results: In the pilot study, 72.2% and 61.1% of early responders (n=18) were responders at 12 and 24 months, respectively; 78.8% of late responders (n=14) were responders at 24 months. In the pivotal trial, of early responders (n=30), 63.3% and 76.7% maintained response at 12 and 24 months, respectively; of late responders (n=40), 65.0% maintained response at 24 months. Early and late responders had fewer treatment changes than nonresponders across the entire pivotal study period. In both studies, analyses of serial depression ratings showed stable symptomatic improvement in early and late responders.

Conclusion: These patients had exceptional levels of chronicity and treatment resistance. Yet patients who showed substantial clinical benefit early or late after starting VNS maintained the improvement at remarkably high rates. This durability of benefit was not attributable to alterations in other treatments.

References:

1. Rush AJ, Sackeim HA, Marangell LB, et al: Effects of 12 months of vagus nerve stimulation in treatment-resistant depression: a naturalistic study. Biol Psychiatry. 2005; 58:355-363.
2. Nahas Z, Marangell LB, Husain MM, et al. Two-year outcome of vagus nerve stimulation (VNS) for treatment of major depressive episodes. J Clin Psychiatry. 2005; 66:1097-1104.

NR188 Monday, May 22, 3:00 PM - 5:00 PM

Neuropsychological Aspects of Lack of Insight in Patients With Bipolar Disorder in Remission

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Educational Objectives:

At the conclusion of this presentation, the participant should gain knowledge on the relationship between insight and neuropsychological functions in bipolar disorder, as well as the cerebral areas possibly involved in the generation of insight mediated mechanisms.

Summary:

Objective: Our aim was to investigate the relationship between insight dimensions and neuropsychological function in outpatients with bipolar disorder in remission.

Methods: We administered the shortened version of the Scale to Assess Unawareness of Mental Disorder (SUMD) and a neuropsychological test battery to a sample of 21 bipolar patients in remission.

Results: We found a positive association between global insight and awareness for a mental disorder, and a test of mental control (Digit Span), indicating that subjects with better scores on this test had more intact insight. There was also a positive association between awareness for the social consequences of the disease, and a modest negative association between awareness for the medication effects on tests of perceptual-motor skills (SDMT and TMT-A), indicating that subjects with better scores on these tests had more intact insight. No significant association was found between the various dimensions of insight and the results of other neuropsychological tests, or other variables like age, education, age of disease onset or duration, and number of hospitalizations.

Conclusions: The relationship between several insight dimensions and neuropsychological functions in remitted bipolar patients was only evident in tests of mental control and perceptual-motor skills. Based on Pet-Scan studies, we found these tests activate four Brodman Areas - BA6, BA45, BA8 and BA9 - which are all part of the human frontal cortex, lending support to the hypothesis that good insight in bipolar disorder is at least partially dependent on intact frontal-executive functioning.

References:

1. Amador X, David A: Insight and Psychosis. New York, Oxford University Press, 2004.
2. Yen CF, Chung LC, Chen CS: Insight and neuropsychological functions in bipolar outpatients in remission. J Nerv Ment Dis 2002;190(10):713-715.

NR189 Monday, May 22, 3:00 PM - 5:00 PM

Olanzapine/Fluoxetine Combination Versus Lamotrigine in the Long-Term Treatment of Bipolar I Depression

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Educational Objectives:

At the conclusion of the session, the participant should be able to discuss the relative merits of OFC and LMG for the long-term treatment of bipolar I disorder, depressed.

Summary:

Objective: To determine efficacy and tolerability of olanzapine/fluoxetine combination (OFC) compared with lamotrigine (LMG) for long-term treatment of bipolar I depression.

Methods: This 25-week randomized, double-blind study compared OFC (6/25, 6/50, 12/25, or 12/50 mg/day, N=205) with LMG titrated to 200 mg/day (N=205) in patients with bipolar I disorder, depressed. Outcome measures included Clinical Global Impres-

sion Severity (CGI-S) (primary), Montgomery-Åsberg Depression Rating Scale (MADRS), and Young-Mania Rating Scale (YMRS) total scores.

Results: OFC-treated patients had significantly greater improvement than LMG-treated patients across the 25-week treatment period on CGI-Severity (p=.008), MADRS (p=.005), and YMRS (p<.001). Time to response (MADRS decrease ≥50%) was significantly shorter for OFC-treated patients (21 versus 33 days, p=.013). For patients in remission (MADRS≤12) after the 7-week acute phase, the subsequent 18.2% (14/77) LMG versus 13.7% (13/95) OFC relapse rate (MADRS>15) was not significantly different by treatment (p=.528). The rate of treatment-emergent mania was 7.3% (14/191) versus 5.0% (10/202) for LMG- versus OFC-treated patients (p=.401). OFC-treated patients had more frequent (p<.05) somnolence, increased appetite, dry mouth, sedation, weight gain, and tremor; and LMG-treated patients had more frequent insomnia. There was a significant difference in incidence of treatment-emergent cholesterol ≥240: OFC 15.9% versus LMG 3.7% (p<.001) and weight gain of ≥7%: OFC 33.8% versus LMG 2.1% (p<.001).**Conclusions**: Patients with acute bipolar I depression had significantly greater symptom improvement over 25 weeks on OFC compared with LMG. There was no treatment difference in relapse rate. OFC-treated patients had more treatment-emergent adverse events, high cholesterol, and weight gain.

References:

1. Tohen M, Vieta E, Calabrese J, et al: Efficacy of olanzapine and olanzapine/fluoxetine combination in the treatment of bipolar I depression. [erratum appears in Arch Gen Psychiatry 2004 Feb;61(2):176]. Arch Gen Psychiatry 2003; 60(11):1079-88.
2. Calabrese JR, Bowden CL, Sachs GS, et al: A double-blind placebo-controlled study of lamotrigine monotherapy in outpatients with bipolar I depression. J Clin Psychiatry 1999; 60:79-88.

NR190 Monday, May 22, 3:00 PM - 5:00 PM

Effects of Lithium on the HPA Axis in Patients With Unipolar Major Depression

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Educational Objectives:

At the conclusion of this presentation, the participant should know about the effects of lithium on the HPA axis in unipolar depressed humans and about the method of the combined dexamethasone/CRH test.

Summary:

Objective

(I) Profound alterations of the hypothalamic-pituitary-adrenocortical (HPA) axis regulation were repeatedly shown in depressed patients. The most sensitive challenge test of the HPA axis, the combined dexamethasone/CRH test (DEX/CRH test), shows an overstimulation of ACTH and cortisol in depressed patients. Under tricyclic antidepressant treatment, a normalization of the HPA axis overdrive was found to precede the clinical improvement. (II) Lithium is a well established drug for the treatment of affective disorders. Yet, its exact mode of action and its effects on the HPA axis are still unknown.

Design and Methods

Three 4-week studies with each 30 acutely depressed patients (unipolar, SCID I confirmed) were conducted. In study 1, patients refractory to a treatment trial with an antidepressant of at least four weeks were treated with lithium augmentation. In study 2 and 3, drug free patients were treated with lithium monotherapy or citalopram monotherapy respectively. Weekly HAM-D ratings were performed. In each study, the DEX/CRH test was conducted right before and four weeks after initiation of the pharmacotherapy.

Results

All three pharmacological strategies showed good antidepressive efficacy. Both lithium monotherapy and lithium augmentation led to a (for most parameters significant) increase in the HPA axis activity. In contrast, citalopram monotherapy resulted in a decrease of the hormone response to the DEX/CRH test.

Conclusion

Lithium has HPA axis activating effects in depressed subjects. This is in line with results of former laboratory and animal studies. Study 3 showed that this effect is not simply related to serotonergic effects. A down-regulation of the HPA axis does not seem to be a necessary prerequisite of an effective antidepressive drug response.

References:

1. Bschor T, Lewitzka U, Sasse J, Adli M, Köberle U, Bauer M: Lithium augmentation in treatment-resistant depression: clinical evidence, serotonergic and endocrine mechanisms. Pharmacopsychiatry 2003;36 (Suppl 3):230-234.
2. Bauer M, Döpfmer S: Lithium augmentation in treatment-resistant depression - A meta-analysis of placebo-controlled studies. J Clin Psychopharmacol 1999;19:427- 434.

NR191 Monday, May 22, 3:00 PM - 5:00 PM

A Comparison of Tolerability Profiles of Patients With MDD Receiving SSRIs in a Naturalistic Clinical Care Setting

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Educational Objectives:

At the conclusion of this presentation, the participants should be able to understand the similarities and differences in side effect profiles of approved selective serotonin reuptake inhibitors used for the treatment of patients with major depression in clinical practice.

Summary:

Objectives: Most of the data regarding side effects of SSRIs are derived from short term research trials with protocol-driven entry criteria. The objective of this study is to compare the tolerability of monotherapy with SSRIs in patients with a MDD in a real-world clinical setting.

Methods: Data were captured by the Clinical Research Information System (CRIS) from 1999 through 2004 at the Duke University Medical Center. CRIS is an Electronic Psychiatric Medical Record Repository tool used for all clinical and research activities. The Study Cohort included 2292 with MDD who received SSRI monotherapy and attended at least 2 visits. Tolerability measures included physicians' assessments of side effects and the duration of treatment and compared across sertraline (n=719), citalopram (n=431), escitalopram (n=298), fluoxetine (n=499), and paroxetine (n=345) groups.

Results: Medications were generally well tolerated. The highest rates for any side effects were for citalopram (27%) followed by paroxetine (23%), escitalopram (19%), fluoxetine (19%), and sertraline(15%) (chi-square =23.07, p<.001; p<.05 for sertraline versus citalopram and sertraline versus paroxetine). Comparisons favored sertraline over citalopram for nausea, sedation and sexual dysfunction (all p values <.05) and and sertraline over paroxetine for sexual dysfunction (p<.05). There were no significant differ-

ences across the SSRIs for other side effects. Sertraline and fluoxetine had a significantly longer duration of treatment compared to escitalopram (hazards ratio = 1.24, chi-square =5.58, p<.02). The mean doses (mg/day) were: sertraline=118, citalopram=36, escitalopram=17, fluoxetine=41, paroxetine=34.

Conclusion: SSRIs were generally well tolerated in a major depressed cohort in a clinical setting. However, compared to sertraline, citalopram patients appear to experience higher rate of side effects, in particular nausea, sedation, and sexual dysfunction; and paroxetine patients experience more sexual dysfunction.

References:

1. Masand PS, Gupta S: Selective serotonin-reuptake inhibitors: an update. Harv Rev Psychiatry 1999; 7:69-84.
2. Goldstein BJ, Goodnick PJ: Selective serotonin reuptake inhibitors in the treatment of affective disorders--III. Tolerability, safety and pharmacoeconomics. J Psychopharmacol 1998; 12(3 Suppl B):S55-87.

NR192 Monday, May 22, 3:00 PM - 5:00 PM

Escitalopram Significantly Improves Core Symptoms of Depression

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Educational Objectives:

At the conclusion of this presentation the participant should be able to recognize the importance of analyzing the effects of treatment on the core symptoms of depression, like depressed mood and melancholic features, and understand the data showing the efficacy of escitalopram in improving the core features of depression.

Summary:

Introduction

Depressed mood and melancholic features are recognized as core symptoms of depression. Escitalopram is the most selective 5HT reuptake inhibitor (SSRI) indicated for MDD or GAD.

Methods

Four 8-week, randomized, double-blind, placebo-controlled trials of escitalopram 10-20 mg/day in adults have prospectively assessed the HAMD, HAMD depressed mood item, and the 6-item HAMD melancholia subscale[1] (depressed mood, guilt, work and activities, retardation, psychic anxiety, and general somatic symptoms) as protocol-defined secondary endpoints. Male or female outpatients had moderate-to-severe DSM-IV-defined MDD (baseline MADRS≥22 for three trials, baseline 24-item HAMD≥25 for the fourth trial).

Results

Three of the four trials demonstrated separation of escitalopram from placebo at week 8 in the primary efficacy measure of MADRS total score; in the fourth trial, both escitalopram and the active control failed to separate from placebo. In all 4 trials, escitalopram was significantly superior to placebo in change from baseline at week 8 for both HAMD depressed mood and HAMD melancholia subscale (OC; for LOCF, this occurred in three of the trials). When all 4 trials were pooled, each component item of the HAMD melancholia subscale was significantly improved by escitalopram versus placebo ($p<0.05$), and the LSMD [95%CI] at week 8 (LOCF) for the HAMD melancholia subscale for escitalopram (N=639) versus placebo (N=527) was -1.37 [-1.84, -0.89].

Conclusion

Escitalopram has a consistent effect on the core symptoms of depression.

References:

1. Bech P, Allerup P, Gram LF, Reisby N, Rosenberg R Jacobsen O, Nagy A. The Hamilton depression scale: evaluation of objectivity using logistic models. Acta Psychiatr Scand. 1981;63:290-299.
2. Burke WJ, Gergel I, Bose A. Fixed-dose trial of the single isomer SSRI escitalopram in depressed outpatients. J Clin Psychiatry. 2002; 63:331-336.

NR193 Monday, May 22, 3:00 PM - 5:00 PM

Can Deterioration of Lithium Response With Discontinuation During Long-Term Prophylaxis Be Predicted?

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Educational Objectives:

to discuss lithium prophylactic treatment, and clinical predictors of response deterioration in long term follow up

Summary:

Introduction:

It is known that one third of bipolar patients show inadequate response to lithium prophylaxis. In good response group, some patients show deterioration in lithium response. There are some observations that lithium discontinuation may cause response change and resistance. The aim of this study is to investigate the predictors and clinical variables for deterioration of lithium response.

Methods:

The life charts of patients with bipolar disorders (DSM IV, bipolar I and II) were reviewed. At least one year lithium monotherapy prophylaxis before discontinuation and after restarting, existence of clear opinion about response type were inclusion criteria. Patients were assigned to two groups after discontinuation and restarting lithium; 1. worsening of the response 2. no response change .

Sociodemographics, clinical variables, discontinuation characteristics were compared between the groups.

Results:

56 patients and 67 discontinuation protocols (16 response worsening, 51 no response change) were included in study. There were no difference on duration of prophylaxis, number and types of mood episodes and discontinuation features between the groups.

Discussion:

Even though we did not find any clinical predictors, future studies at neurocelular and biological markers may predict response deterioration .

References:

1. Lithium discontinuation and subsequent effectiveness. Coryell et al.,Am J Psychiatry. 1999 Jul;156(7):1130.
2. The clinical effects of lithium discontinuation: the debate continues. MacQueen G, Joffe RT. Acta Psychiatr Scand. 2004 Feb;109(2):91-5.

NR194 Monday, May 22, 3:00 PM - 5:00 PM

Quetiapine in the Treatment of MDD in Elderly Patients With Cerebrovascular Damage

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Educational Objectives:

At the conclusion of this session, the participants should familiar with preliminary data on the efficacy of quetiapine combination therapy for the treatment of depressed elderly patients with cerebrovascular damage.

Summary:

Background: Depressive episodes in elderly patients with cerebrovascular damage are characterized by poor responses to standard antidepressants. Recent reports have suggested that the bimodal mood stabilizer quetiapine may have antidepressant properties.

Objective: To evaluate the efficacy of combination therapy with quetiapine in depressed elderly patients with cerebrovascular damage.

Method: An open-label, 6-month, follow-up study of patients with MDD (DSM-IV) and cerebral abnormalities (assessed by MRI) without severe cognitive impairment. Patients who had not responded to standard antidepressants (mean [SD] months of treatment 6.5±7.2) additionally received quetiapine (300±111 mg/d). Patients were evaluated at baseline (t0) and Months 1, 3, and 6 (t1, t3, t6) using the Clinical Global Impression Scale for Severity (CGI-S) and the Hamilton Depression Rating Scale (HAM-D).

Results: Nine patients were included in the study, with a mean age of 72.8±9.4 years. CGI-S scores decreased from baseline to Month 6: 5.8±0.7 (t0), 5.4±0.7 (t1), 5.0±0.8 (t3), and 4.5±1.0 (t6), with a significant improvement at 6 months compared with baseline (P=0.006). A significant improvement over the 6-month period was also observed with HAM-D scores (t0=27.2±4.0, t6= 14.8±3.8, P<0.0001).

Conclusions: These results show that quetiapine is efficacious as combination therapy in depressed elderly patients with cerebrovascular damage. The promising results from this study warrant confirmation in large, randomized, double-blind, placebo-controlled studies.

Supported by funding from AstraZeneca Pharmaceuticals LP.

References:

1. Calabrese JR, Keck PE, Jr., Macfadden W, Minkwitz M, Ketter TA, Weisler RH, et al. A randomized, double-blind, placebo-controlled trial of quetiapine in the treatment of bipolar I or II depression. Am J Psychiatry 2005;162(7):1351-60.
2. Hardoy MC, Garofalo A, Carpiniello B, Calabrese JR, Carta MG. Combination quetiapine therapy in the long-term treatment of patients with bipolar I disorder. Clin Pract Epidemol Ment Health 2005;1:7.

NR195 Monday, May 22, 3:00 PM - 5:00 PM

Major Depressive Disorder Among Emergency Department Patients in Latin-American Countries

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Educational Objectives:

Demonstrate the importance of identifies depressive disorders among patients in Emergency Departments (ED)

Recognize the characteristics of depressive patients in ED

Summary:

Objective: This multi-center study estimated the prevalence of MDD among emergency department (ED) patients in Latin American countries.

Methods: Using an interview and a questionnaire screen including the center for Epidemiological Studies Depression Scale (CES-D), we analyzed data from consecutive adult patients from hospitals in Argentina, Brazil, Chile, Colombia, and Mexico and described the demographic and health status differences between depressed and non-depressed patients.

Results: Prevalence for MDD range from 23.0% to 35.0%. The estimates are based on a total of 1,835 patients aged 18 and over, with response rates of 83.0% .Compared to non-MDD patients, MDD patients were more likely to be middle-aged, female, smokers, of lower socioeconomic status, and to report a diagnosis of asthma or arthritis/rheumatism. Multivariate analysis identified lower level of education, smoking, and self-reported anxiety, chronic fatigue, and back problems to be independently associated with MDD.

Conclusions: Our data suggest that the prevalence of MDD is elevated among ED patients in Latin-American countries. The integration of depression screening into routine emergency care merits serious consideration, especially if such screening can be linked to psychiatric treatment

References:

1. Babcock Irvin, C., Wyer, P. C., & Gerson, L. W. (2000). Preventive care in the emergency department, Part II: Clinical preventive services--an emergency medicine evidence-based review. Society for Academic Emergency Medicine Public Health and Educati.
2. Dahlen, I., & Janson, C. (2002). Anxiety and depression are related to the outcome of emergency treatment in patients with obstructive pulmonary disease. Chest, 122(5), 1633-1637.

NR196 Monday, May 22, 3:00 PM - 5:00 PM

Genetic Variability at the SERT Gene Interacts With Social Adversity Increasing the Risk for Depression: Evidence From a Spanish Cohort

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to:

1) Gain exposure to further evidence on the importance of genetic/environmental interaction in the emergence of depression

2) Understand that certain gehotypes of the SERT gene seem to convey higher risk for depression

3) Understand that social adversity measured in the form of "previous threatening life-events" is also associated with depression in our sample.

4) Getting some evidence of an empiric al demonstration of SERT genotype/Life-Events interaction in depression.

Summary:

Background: Caspi et al (2003) reported a GxE interaction between the s/s genotype at the SERT locus and priorly suffered life-evets (LEs) in association with depression.

Objective: The Predict-Gene study sets out to replicate such findings using a primary-care sample from Andalusia (Spain).

Methods: 555 patients who consecutively gave informed consent were included in the study. Depression was established using the CIDI depression subscale whilst control status was determined by CIDI, GHQ and absence of psychiatric family history. Exposure to LEs during the previous 6 months was gathered using the List of Threatening Experiences by Brugha (1990). A blood sample

was also obtained to extract DNA and determine the SERT genotype profile (s/s, s/l or l/l).

Results: 480 subjects (141 depressed and 339 controls) were included following exclusion of non-depressed subjects who did not qualify as valid controls. Among the depressed patients 32% had the higher risk s/s genotype compared to 22% of controls (OR=1.62; 95%CI:1.05-2.5; p=0.037). Having two or more LEs was also significantly higher amongst the depressed (54%) compared to controls (31%) (OR=3.37; 95%CI:1.96-5.77; p=0.0001). When exploring the likelihood ratio for the interaction between the SERT genotype and exposure to LEs, we found a nearly significant result showing a SERT by LEs interaction (LR Chi2=5.48, p= 0.06). Thus, whilst among s/s subjects the risk for depression was significantly higher after exposure to just one LE, those subjects with l/l or l/s genotype required a greater degree of exposure to LEs (2+) for a similar level of risk for depression (Test for different probabilities accross all levels of exposure: LR Chi2=34.41; p<0.0001).

Conclusion: Our findings do support that SERT genotype interacts with LEs to increase risk for depression.

Acknowledgements: We thank the Predict Study Core Group for allowing us to use local Spanish clinical data for this study.

References:

1. Caspi,A.; Sugden,K.; Moffitt,T.E.;et al. Influence of life stress on depression: moderation by a polymorphism in the 5-HTT gene. Science 2003; 301:386-389.
2. Brugha, TS & Cragg, D. The List of Threatening Experiences: The reliability and validity of a brief life events questionnaire. Acta Psychiatrica Scandinavica, 1990. 82: 77-81.

NR197 Monday, May 22, 3:00 PM - 5:00 PM

Subthalamic Deep Brain Stimulation in Parkinson's Disease and Mood Disorders, One-Year Follow-Up

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Educational Objectives:

At the conclusion of this presentation, the participant should be abble to know that subthalamic stimulation in Parkinson's disease, could induce mood disorders.

Summary:

Objectives :

Several cases of transient acute depression or manic symptoms are reported in the literature after bilateral subthalamic nucleus (STN) deep brain stimulation in patients with Parkinson's disease. We have few data about their frequency or cause. Different hypothesis involve premorbid personality disorders or thymic past history. Another hypothesis involve subthalamic nucleus.

Methods : We elaborate a one year prospective study to evaluate mood disorders frequency and physiological mechanisms of 20 Parkinsonian patients treated by bilateral STN stimulation. We enroled in our sample the 20 first consecutive Parkinsonians who were selected to be operated. Evaluation consist of pre and post-operative psychiatric interview and scales : Montgomery and Asberg Depression Rating Scale (MADRS), Mini International Neuropsychiatric Inventory (MINI), Scale Inventory Personality Disorder (SIPD), Mania Assessment Scale (Bech), Assessment of Depression (Beck), Apathic scale and neuropsychologic tests.

Results: After one year, among 18 operated patients, temporary results show one case of hypomania with behavioral disorder (DSM-IV criteria). This patient, without thymic history, presented a paranoid personality disorder. Using tools, we did not identified in the others 17 patients, acute depression or manic symptoms, but seven cases of discordance since auto and hetero evaluation on depressive symptoms.

Conclusion : Data are still on analysed, but this case draw our attention to the effects of STN stimulation on mood and behavioural disorders. The difference since auto and hetero evaluation in depressive symptoms may be related with problem of insight. Lastely importance of psychiatric follow-up is revelated by these results.

References:

1. Krack P, Batir A, Van Blercom, N, Chabardes S, Fraix V, Ardouin C, Koudsie A, Dowsey Limousin P, Benazzouz A, Lebas JF, Benabid, AL, Pollak P. Five-Year Follow-up of Bilateral Stimulation of Subthalamic Nucleus in Advanced Parkinson's Disease.
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NR198 Monday, May 22, 3:00 PM - 5:00 PM

Neurocognitive Function in Patient With Hwa-Byung and MDD

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Educational Objectives:

These results suggest that both HB group and MDD group have significantly decreased neurocognitive function than control group, and neurocognitive function of MDD group is lower than HB group

Summary:

Objectives

Hwa-byung has been studied clinically for several years and introduced as Korean Culture-Bound Syndrome. However, the definition and the diagnostic method are not yet clarified, and there has not been any sufficient comparative study on this disease entity.

We wished to determine the clinical symptoms and the profile of the neuro-cognitive functions disturbed in Hwa-byung(HB) and MDD(MDD), and identify any critical factors that differentiate the disorders.

Methods

A total of 102 participants were examined, including 34 participants with MDD, 34 with HB, 34 with healthy controls. The MDD and HB patients were recruited from among inpatients and outpatients at the National Medical Center for the period from May to December of 2004.

As a major diagnostic tool of MDD, diagnostic reference of DSM-IV-TR was used and as HB's diagnostic tool.

Results

MDD and HB groups showed significantly higher total scores on the SCL-90-R in comparison to the controls. MDD group was found to have significantly more symptoms of depression than HB group, based on the depression subscale of the SCL-90-R.

The computerized neurocognitive function test suggest several results 1) Within the memory domain, it was found that one of the two memory tests in MDD and HB groups were significantly impaired in comparison to control group. 2) Within the attention domain, it was found that only MDD group was significantly impaired in comparison to the control group. 3) Within the higher cortical function domain, it was found that significant impairment exist in MDD group and HB group compared to the control group; the severity of impairment was found to be more profound in MDD group than HB group.

Conclusion

These results suggest both HB group and MDD group have significantly decreased neurocognitive function than control group, and neurocognitive function of MDD group is lower than HB group.

References:

1. Sung Kil Min, Kee Namkoong, Ho Young Lee(1990): An Epidemiological Study the on Hwabyung. J Korean Neuropsychiatr Assoc 29:867-874.
2. Jong Woo Kim(2004): Hwabyung in Oriental Medicine, Behavioral Science in Medicine 3: 103-107.

NR199 Monday, May 22, 3:00 PM - 5:00 PM

Sexual Functioning in Long-Term Treatment of MDD: Duloxetine, Escitalopram, and Placebo

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Educational Objectives:

At the completion of the presentation, the participant will understand differences in sexual functioning associated with antidepressants with different mechanisms of action versus placebo.

Summary:

Background: Depression and antidepressant therapy have been associated with sexual dysfunction in short term and point-prevalence trials. This report describes effects on sexual functioning during long-term treatment for depression.

Methods: This 8-month, double-blind, placebo-controlled study of duloxetine and escitalopram had 2 phases: a) an 8-week acute phase, fixed-dose, comparison of duloxetine 60 mg/d (n=273), escitalopram 10 mg/d (n=274), and placebo (n=137); and b) a 6-month, flexible dose extension phase (duloxetine, 60, 90, or 120 mg/d; escitalopram, 10 or 20 mg/d; placebo rescue to active drug) based on pre-defined criteria. The 14-item self-report Changes in Sexual Functioning Questionnaire (CSFQ) was used to assess sexual function.

Results: Statistically significant worsening of sexual functioning as measured by the CSFQ was observed for escitalopram versus placebo at 4 and 8 weeks ($p<.01$), while duloxetine was not statistically different from placebo at anytime. There was a statistically significant difference for duloxetine versus escitalopram at 12 and 16 weeks ($p<.05$). This was confirmed with the Quality of Life Enjoyment and Satisfaction Questionnaire-SF which demonstrated an advantage during the 8-month study for duloxetine over escitalopram in satisfaction with sexual drive, interest, and /or performance ($p=.013$). At 8 weeks, categorical changes in sexual function (same, better or worse) on the CSFQ differed significantly for duloxetine versus escitalopram ($p=.019$) in male patients, with no significant difference between active drugs in females. At 8 months, there were no statistically significant differences observed between duloxetine and escitalopram in categorical changes on the CSFQ for male or female patients. Discontinuation rates for sexual side effects did not differ for duloxetine (n=2) versus escitalopram (n=7, $p=.07$).**Conclusions:** Short-term treatment demonstrated worsening of sexual functioning with escitalopram as compared to placebo, while duloxetine was not significantly different from placebo at anytime during the 8-month study. Funding provided by Eli Lilly and Company

References:

1. Clayton AH, Pradko JR, Croft HA, et al. Prevalence of sexual dysfunction among newer antidepressants. J Clin Psychiatry 2002;63:357-366.
2. Delgado P, Brannan S, Mallinckrodt C, et al. Sexual functioning assessed in 4 placebo- and paroxetine-controlled trials of duloxetine for major depressive disorder. J Clin Psychiatry 2005;66:686-692.

NR200 Monday, May 22, 3:00 PM - 5:00 PM

Finding a Silver Lining: Benefit Finding in Bipolar Disorder

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize benefit finding and its relationship to coping with bipolar disorder.

Summary:

Objective: To assess benefit-finding in individuals with bipolar disorder (BD) whose mood is euthymic.

Method: Forty-seven participants (age 44.3±12.5; 57% female) diagnosed with BD using the Systematic Treatment Enhancement Program (STEP-BD) Affective Disorders Evaluation (ADE), euthymic for at least two months, completed self-report questionnaires as part of an ongoing longitudinal survey of psychosocial aspects of coping with BD.

Results: Participants reported finding benefits from their experiences with BD. Ratings for 23 possible benefits were made on a scale ranging from 1 ("not at all") to 5 ("extremely"). Benefits were coded as endorsed if rated at least 3 ("moderately"). Participants endorsed an average of 13.8±6.06 of the 23 benefit items, with the most strongly reported benefits including: "Having had BD .has made me more understanding of others who have problems" (endorsed by 85% of participants; overall M=3.83±1.14), "has increased my self-awareness," (81%, overall M=3.72±1.18), "has helped me become a stronger person, more able to cope effectively with future life challenges" (69%, overall M=3.48±1.32), "has led me to be more accepting of things" (68%, M=3.41±1.31), and "has helped me become more focused on priorities, with a deeper sense of purpose in life" (65%, overall M=3.22±1.41). Non-Caucasian participants tended to report greater levels benefit-finding than Caucasian participants ($p=.07$). Benefit-finding correlated positively with use of coping skills including self-distraction, use of emotional support from friends, use of instrumental support, venting, positive reframing, humor, acceptance, emotional processing, and emotional expression (all *ps<.02).*

Conclusion: Findings suggest that euthymic individuals diagnosed with BD commonly identify benefits associated with the disorder and that use of coping skills relates to the ability to find positive aspects of having experienced BD. This project represents an important step in elucidating specific psychosocial factors associated with resilience and positive psychological functioning in individuals with bipolar disorder.

References:

1. Carver CS, Antoni MH: Finding benefit in breast cancer during the year after diagnosis predicts better adjustment 5 to 8 years after diagnosis. Health Psychology 2004; 23, 595-598.
2. Pakenham KI: Benefit finding in multiple sclerosis and associations with positive and negative outcomes. Health Psychology 2005; 24, 123-132.

NR201 Monday, May 22, 3:00 PM - 5:00 PM

The Prevalence and Clinical Consequences of the Metabolic Syndrome in Patients With Bipolar Disorder

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Educational Objectives:

Appreciate the high prevalence and clinical consequences of metabolic disorders in patients with bipolar disorder.

Understand the pathogenesis of medical comorbidities such as diabetes and cardiovascular disorders in patients with bipolar disorder.

Acquire skill in the prevention, recognition and management of metabolic disorders in patients with bipolar disorder.

Summary:

Introduction: Patients with bipolar disorder suffer greater medical morbidity and mortality from cardiovascular disorders than others in the general population. **Objective**: The purpose of the present study was to evaluate the prevalence and clinical consequences of the metabolic syndrome in patients with bipolar disorder. **Methods:** We recruited 41 patients with bipolar disorder, who were consecutively admitted to the psychiatric unit of a general hospital in mid-Michigan in a manic or mixed state, during calendar years 2004 and 2005. We retrieved demographic and clinical information. We used admission Young Mania Rating Scale scores and hospital lengths of stay as measures of illness severity. **Results:** Fifty-sixty percent of the sample met modified NCEP ATP III criteria for the metabolic syndrome, 41% were obese, 71% displayed dyslipidemia, 62% were hypertensive, and 48% were diabetic or pre-diabetic. The mean lengths of hospital stays and YMRS scores were higher in patients with obesity, dyslipdemia, diabetes or pre-diabetes, and the metabolic syndrome than for healthier individuals. **Conclusions**: The prevalence of the metabolic syndrome in patients hospitalized with bipolar disorder was dramatically higher than the prevalence observed in community samples. The magnitude of co-morbid metabolic disorders correlated positively with the severity of the mood disorder.

References:

1. Kupfer DJ: The Increasing Medical Burden in Bipolar Disorder. JAMA 2005; 293 (20):2528-2530.
2. Fagiolini et al.: Metabolic syndrome in bipolar disorder: findings from the Bipolar Disorder Center for Pennsylvanians. Bipolar Disord 2005: 7: 424'430.

NR202 Monday, May 22, 3:00 PM - 5:00 PM

Mapping the Effects of Bupropion XL on Negative Emotion Processing in Major Depression

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Educational Objectives:

1. to present results of a fMRI study of a nonserotonergic antidepressant

2. to summarize results of fMRI studies of serotonergic antidepressants

3. to highlight emerging role of fMRI as a surrogate marker of antidepressant efficacy

Summary:

Prior imaging studies suggest that patients with major depression (MD) have alterations in frontal and limbic neural circuitry including the amygdala, in response to negative emotional stimuli (i.e., sadness, fear, etc.). This study used an fMRI paradigm to map the neural correlates of negative emotional response and attentional processing in ten patients with MD (mean HAMD 22) before and after 8 weeks of treatment with bupropion XL. Treatment with bupropion XL was associated with significant improvements in HAMD and CGI ratings ($p<0.05$). Treatment reduced fMRI activation during emotional distracters in several regions including: right orbital frontal cortex, right inferior frontal cortex, right parahippocampal area, right fusiform gyrus, left caudate, and bilateral amygdala. Changes in fMRI activation in the amygdala correlated with improvements on the primary depression rating scale ($p<0.05$). Treatment increased activation to attentional targets in the following regions: right middle and inferior frontal gyri, right caudate, and bilateral precuneus. This pilot study suggests that bupropion XL, a nonserotonergic antidepressant, may attenuate activation in specific emotion-related brain regions and improve activation in specific executive-function networks in association with clinical improvement. fMRI surrogate markers offer promise for studying neural correlates of antidepressant therapies.

References:

1. Wang L et al. Amygdala activation to sad pictures during high field fMRI. Emotion 2005; 5:12-15.
2. Morris JS et al. Differential neural response in amygdala to fearful and happy facial expressions. Nature 1996;383:812-814.

NR203 Monday, May 22, 3:00 PM - 5:00 PM

Spectrum of Executive Dysfunction in Vascular Depression: Duke-Washington University Collaborative Study

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Educational Objectives:

1. to review emerging relevance of executive function and vascular changes in late life depression

2. to present new data on patterns of executive function in outpatients with vascular versus nonvascular depression

3. to present the results from the ongoing Duke Washington University collaborative NIMH clinical trial of late life depression

Summary:

Executive dysfunction in geriatric depression has been reported to increase the risk for poor outcomes, particularly after treatment with SSRIs. The initiation preservation (IP) subscale of the Dementia Rating Scale has been proposed as a simple office based measure of executive function. The Duke-Washington University collaborative study is a prospective NIMH funded outpatient clinical trial that examines the efficacy of sertraline in vascular versus nonvascular depression. We report here an interim analyses of the spectrum of executive function at baseline in these subjects. 176 nondemented patients (mean MMSE=27.7, sd=2) with major depression (mean MADRS=25.6, sd=5.6), from two sites, underwent baseline MRI scans (for ratings of cortical and subcortical brain changes to categorically classify the patients as vascular versus nonvascular depression) and IP testing. 101 (57%) patients met MRI criteria for vascular depression. At baseline, vascular depressives were older ($p<0.0001$) and tended to have higher MADRS ($p<0.06$) and lower MMSE ($p<0.07$) scores than nonvascular patients. IP scores were associated with baseline MADRS

ratings of depression severity (p=0.056). 73% of nonvascular depression patients had an IP score of 37 compared to 41% of those with vascular depression (p<0.05). The relationship between IP and MRI ratings was not significant after adjusting for age and depression severity. These findings will be presented and discussed in relation to the growing prognostic significance of executive dysfunction in geriatric depression.

References:

1. Doraiswamy PM, Sheline Y. Vascular depression. in Depression in Later Life (Eds JM Ellison, S Verma), Marcel Dekker, NYC, 155-167, 2003.
2. Taylor W, Doraiswamy PM. Systematic review of controlled antidepressant clinical trials for geriatric depression: Limitations of current data and directions for future. Neuropsychopharmacology, 2004, 29:2285-2292.

NR204 Monday, May 22, 3:00 PM - 5:00 PM

Efficacy of Aripiprazole in the Treatment of Bipolar Depression

Robert T. Dunn, M.D. *Cambridge Health Alliance, 1493 Cambridge Street, Cambridge, MA, 02139*, Benjamin Zablotsky, B.A., Vanessa A. Stan, A.B.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to determine the efficacy of aripiprazole in the treatment of acute bipolar depression.

Summary:

Objective: A previous published study (1) indicates that aripiprazole, a novel neuroleptic (2), is effective in the treatment of mania. This first prospective study investigated the efficacy and safety of aripiprazole in bipolar depression.

Method: An open label, prospective, non-randomized, 6-week study was conducted in bipolar outpatients (type I, type II, or NOS), depressed phase. Previous treatments were continued unchanged, but no new treatments were allowed. Montgomery Asberg Rating Scale (MADRS) and the Mania Rating Scale (MRS) from the SADS-C were used to evaluate depression and manic symptoms respectively. Preliminary analysis of 8 patients was conducted; full data will be presented.

Results: Mean ± SD age was 43.4 ± 8.63 years with 6 males, 2 females (3 BPI, 2 BP II, 2 BP NOS). Doses ranged from 5 to 30 mg/day, with mean endpoint dose 24.3 ± 10.2. Mean MADRS was significantly improved from baseline (23.4 ± 6.5) to endpoint (13.5 ± 8.3) (t= 2.21, p=0.05). Three patients (37.5%) terminated early due to adverse effects, primarily nausea/vomiting.

Conclusion: These preliminary data suggest that aripiprazole is effective in the treatment of bipolar depression.

Funding Source: Supported by Bristol-Myers Squibb Company

References:

1. Keck PE Jr, et al.: A placebo-controlled, double-blind study of the efficacy and safety of aripiprazole in patients with acute bipolar mania. Am J Psychiatry 2003; Sep; 160(9):1651-1658.
2. Burris KD, Molski TF, Xu C, Ryan E, Tottori K, Kikuchi T, Yocca FD, Molinoff PB: Aripiprazole, a novel antipsychotic, is a high affinity partial agonist at human dopamine D2 receptors. J Pharmacol Exp Ther 2002; 302:381-389.

NR205 Monday, May 22, 3:00 PM - 5:00 PM

Efficacy of Divalproex in the Treatment of Acute Bipolar Depression: A Randomized Clinical Trial

Robert T. Dunn, M.D. *Cambridge Health Alliance, 1493 Cambridge Street, Cambridge, MA, 02139*, William S. Gilmer, M.D., Jenelle Fleck, R.N., Benjamin Zablotsky, B.A., Vanessa A. Stan, A.B., Joseph F. Goldberg, M.D., Seyyed N. Ghaemi, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to determine the efficacy of divalproex in the treatment of acute bipolar depression.

Summary:

Objective: The effectiveness of divalproex for mania in bipolar patients is well documented (1). There is, however, only one documented study reporting efficacy of divalproex monotherapy for acute bipolar depression (2). This prospective study will add to the current database available regarding monotherapy of divalproex for bipolar depression.

Method: A double-blinded, stratified placebo-controlled, 6 week study was conducted in bipolar outpatients (type I, type II, or NOS) with depressive symptoms. No psychotropic medications beside divalproex were allowed, and any non-psychotropic medications could not change over the course of the study. The primary outcome measures were the Montgomery Asberg Depression Rating Scale (MADRS) and the Hamilton Depression Rating Scale (HDRS), collected at each clinical visit throughout the study. Two patients (11.1%) terminated early due to adverse effects, including swelling and increased suicidality.

Results: Scores were obtained for 18 patients (9M:9F), with a mean age of 38.7±11.7 years. Bipolar subtypes included 9 BPI, 8 BPII and 1 BP NOS. The blind for this study will be broken and full data on 25 patients will be presented.

Conclusions: The role divalproex plays in treating depressive symptoms in acute bipolar depression will be discussed.

Funding Source: Abbott Laboratories

References:

1. Ghaemi SN: Practical Guides in Psychiatry: Mood Disorders. Philadelphia, PA, Lippincott Williams & Wilkins, 2003.
2. Davis LL, Bartolucci A, Petty F: Divalproex in the treatment of bipolar depression: a placebo-controlled study. J Affect Disord 2005; Apr;85(3):259-266.

NR206 Monday, May 22, 3:00 PM - 5:00 PM

Efficacy and Safety of L-Methionine, Betaine, and Folate in Unipolar Depression

Robert T. Dunn, M.D. *Cambridge Health Alliance, 1493 Cambridge Street, Cambridge, MA, 02139*, Benjamin Zablotsky, B.A., Vanessa A. Stan, A.B.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand the short-term effects of L-methionine, betaine and folate in the treatment of acute unipolar depression.

Summary:

Objective: Prior studies suggest that S-adenosylmethionine (SAMe) is effective in the treatment of unipolar depression (1), and that methionine and betaine can increase SAMe in the brain (2). This first prospective study examined the efficacy and safety of the combination of L-methionine, betaine and folic acid in unipolar depression.

Method: An open label, prospective, non-randomized, 6-week study of fixed doses of methionine, betaine and folate, was conducted in depressed unipolar outpatients. No psychotropic medications were allowed. The Hamilton Depression Rating Scale (HAMD) and the Beck Depression Inventory (BDI) were administered to evaluate depressive symptoms. Furthermore, hepatic

function and sedation rates were obtained. Preliminary analysis of 5 patients was conducted; full data will be presented.

Results: Depression scores were obtained in 5 patients (3M, 2F). Mean HAMD scores improved from baseline (29.0±6.6) to endpoint (11.4±10.0), where (t=3.29, p = 0.01). Mean Baseline BDI scores improved from baseline (27.0±7.1) to endpoint (13.4±7.9), where (t=2.86, p=0.02). There was not a significant increase in sedation rates or change in hepatic functioning.

Conclusion: The combination of L-methionine, betaine and folate has potential to improve acute unipolar depression, without sedation or affecting hepatic functioning. Full data will be presented.

Funding Source: NARSAD

References:

1. Alpert JE, et al.: S-adenosyl-L-methionine as an adjunct for resistant major depressive disorder: an open trial following partial or nonresponse to selective serotonin reuptake inhibitors or venlafaxine. J Clin Psychopharmacol 2004; Dec:24(6):661-664.
2. Baldessarini RJ. Alterations in tissue levels of tissue levels of S-adensylmethionine. Biochem Pharmacol 1966; 15:741-748.

NR207 Monday, May 22, 3:00 PM - 5:00 PM

Identification and Treatment of Psychotic Symptoms in Patients With Bipolar Mania

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Educational Objectives:

At the conclusion of this presentation, the participants should be able to (1) assess the incidence of psychosis in patients with acute bipolar mania and (2) evaluate the efficacy of risperidone in the treatment of manic and psychotic symptoms in these patients.

Summary:

Background: Psychosis has been identified in as many as 68% of patients with bipolar mania. This analysis identified the types of psychotic symptoms present in patients with mania and evaluated the responses to treatment.

Methods: Data were from two placebo-controlled, 3-week studies of risperidone in patients with an acute episode of bipolar mania. Measures included the Positive and Negative Syndrome Scale (PANSS; item ratings, 1=absent to 7=extremely severe) and the Young Mania Rating Scale (YMRS).

Results: Data were available for 515 patients; 264 (51.3%) were diagnosed with psychotic features at baseline. Ratings reflecting delusional content (≥4) on the PANSS grandiosity item were reported in 78% of the patients with psychotic features and in 45% of those without psychotic features. Patients with psychotic features had mean PANSS scores of mild or greater (≥3) on 6 PANSS items: grandiosity (4.5), delusions (4.4), lack of judgment/insight (4.1), excitement (3.9), suspiciousness/persecution (3.1), and hostility (3.1). Patients without psychotic features had scores ≥3 on 3 of the 6 items: excitement, grandiosity, and lack of judgment/insight. In both groups, mean scores at endpoint on each of the 6 PANSS items were significantly lower in patients receiving risperidone than placebo (P<0.001). Mean PANSS total and factor scores (positive symptoms, excitement/hostility, anxiety/depression, and disorganized thought) at endpoint were significantly lower in patients receiving risperidone than placebo (P<0.05). Mean YMRS scores were significantly higher in patients with than without psychotic features at baseline (36.3 ± 7.8 versus 30.6 ± 7.0; P<0.001). Improvements in YMRS scores at endpoint were significantly greater with risperidone than placebo in both patient groups (P<0.001).

Conclusion: These findings support prior reports of high rates of psychosis in patients with bipolar mania. Risperidone was significantly more efficacious than placebo in the treatment of psychotic and manic symptoms in patients with bipolar mania. Supported by Janssen, L.P.

References:

1. Hirschfeld RMA, Keck PE Jr, Kramer M, et al. Rapid antimanic effect of risperidone monotherapy: a 3-week multicenter, double-blind, placebo-controlled trial. Am J Psychiatry 2004;161:1057-1065.
2. Khanna S, Vieta E, Lyons B, et al. Risperidone in the treatment of acute mania: double-blind, placebo-controlled study. Br J Psychiatry 2005;187:229-234.

NR208 Monday, May 22, 3:00 PM - 5:00 PM

Prospective, Long-Term, Multicenter Study of the Naturalistic Outcomes of Patients With Treatment-Resistant Depression

David L. Dunner, M.D. *University of Washington, Department of Psychiatry and Behavioral Sciences, 4225 Roosevelt Way NE, 306C, Seattle, WA, 98105-6099*, A. John Rush, M.D., James M. Russell, M.D., Michael Burke, M.D., Stacy Woodard, Ph.D., Peggy Wingard, M.D., John Allen, Ph.D.

Educational Objectives:

At the conclusion of this presentation, participants should have a better understanding of the characteristics of patients with treatment-resistant depression (TRD) and the long-term outcomes resulting from standard care among this population. These data provide a benchmark for subsequent TRD studies.

Summary:

Objective: We have a poor understanding of the clinical characteristics of patients with treatment-resistant depression (TRD), and have limited evidence for how to best treat this population. This study tracked the outcomes of patients with TRD receiving standard care. These data should provide a benchmark for subsequent TRD studies.

Methods: This 2-year prospective, multicenter, observational study tracked the outcomes of 124 patients with treatment-resistant, nonpsychotic Major Depressive (n=109) or Bipolar depressed phase (n=15) Disorder who received treatment as usual (TAU). TAU consisted of any therapeutic regimen agreed to by the patient and physician, including medications and nonpharmacological treatments such as ECT and psychotherapy. Treatments could be adjusted, started, and stopped as necessary. The primary outcome measurement was response to treatment, defined a priori as ≥50% improvement from baseline as measured by the 30-item Inventory of Depressive Symptomatology-Self-Report (IDS-SR_{30}). The Medical Outcome Survey (MOS) 36-item Short Form Health Survey (SF-36) was used to monitor quality of life changes.

Results: The majority of patients had unipolar (87.9%), recurrent depression (85.3%). The mean baseline IDS-SR_{30} score was 43.8±10.5. The 12- and 24-month IDS-SR_{30} response rates were 11.6% (13/112) and 18.4% (19/103), respectively. Of the 13 responders at 12 months, only five were responders at 24 months. The 12- and 24-month IDS-SR_{30} remission rates were 3.6% (4/112) and 7.8% (8/103), respectively. Only one of the four 12-month remitters was also a remitter at 24 months. The SF-36 indicated globally poor quality of life in this sample.

Conclusions: Despite the wide range of treatment options available for depression, the response rates, remission rates, and

quality of life results observed in this study show that many patients with TRD continue to have significant symptomatology and functional disability when receiving TAU.

References:

1. Rush AJ: Research issues in the study of difficult-to-treat depression. Biol Psychiatry 2003; 53:743-753.
2. George MS: A one-year comparison of vagus nerve stimulation (VNS) with treatment as usual for treatment-resistant depression. Biol Psychiatry 2005; 58:364-373.

NR209 Monday, May 22, 3:00 PM - 5:00 PM

Subtypes of Mania Based on Factor Analysis

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to diagnose manic episode more promptly and clearly.

Summary:

Objective: Manic symptomatological subtypes date back to Kraepelin who divided bipolar illness to manic, depressed, and mixed states. Atypical manic features such as depression, anxiety irritable aggression, and psychosis have sometimes been described as occuring with pure manic features such as euphoria, grandiosity, flight of ideas, and increased drive in some patients with mania. Although early studies on factor analytic subtypes of mania relied on small samples and insufficient rating instruments, numerous later studies addressed dysphoria (depressed mood, lability, guilt, anxiety and suicidal thoughts and behaviours), psychomotor acceleration, psychosis, increased hedonic function and irritable aggression (1,2). In this study we investigated symptomatological subtypes of mania based on factor analysis in DSM-IV bipolar disorder manic or mixed episodes with or without psychotic features.

Method: One hundred and eleven consecutive inpatients with DSM-IV manic or mixed episodes with or without psychotic features were recruited in Bakirkoy State Training and Research Hospital for Psychiatry and Neurology. Patients were rated in three days of hospitalization with Structured Clinical Interview for DSM-IV (SCID), Young Mania Rating Scale, Montgomery Asberg Depression rationg scale and Assessment of Positive Symptoms Scale. A principal-component analysis followed by varimax rotation was conducted for the 24 psychiatric symptoms at admission.

Results: This analysis revealed six factors which explained 63% of the total variance. First factor was dysphoria (21.9%), and others were psychomotor acceleration (15.9%), psychosis (8.1%), irritability (6.7%), paranoia and hostility (5.4%), insight factors (4.8%).

Conclusions: Our data supports the multidimensional phenomenology of mania in contrast to classic definition of euphoric-grandiose (2).

References:

1. Akiskal HS, Azorin JM, Hantouche EG: Proposed multidimensional structure of mania: beyond the euphoric-dysphoric dichotomy. J Affect Disord 2002; 73: 7-18.
2. Cassidy F, Pieper CF, Carroll BJ: Subtypes of maniz determined by grade of membership analysis. Neuropsychopharmacology 2001; 25: 373-383.

NR210 Monday, May 22, 3:00 PM - 5:00 PM

Bipolar Disorder

Angelo Fallu, M.D. *Clinique Woodward, 685, rue Woodward, Sherbrooke, PQ, J1G 1W4, Canada*, Carin Binder, Lakshmi N. Yatham, M.D.

Educational Objectives:

1. At the conclusion of this presentation, the participant should be able to make an informed choice as to treatment with a long acting stypical injectable.
2. At the conclusion of this presentation, the participant should be able to have an understanding of the side effect profile of antipsychotics used in adjunct treatment.

Summary:

Objective: To determine the safety of long acting injectible risperidone (LAIR) in bipolar subjects randomly assigned to continue current adjunct atypical antipsychotic (AAP) OR initiate treatment with LAIR.

Methods: Open-label, randomized study of 6 months duration. Forty subjects with Bipolar Disorder treated with an atypical antipsychotic (risperidone, quetiapine, olanzapine) plus adjunct treatment consisting of a combination of one or two mood stabilizers; and, if applicable, one antidepressant were eligible to be enrolled once they signed consent. Subjects randomized to LAIR were initiated on 25 mg with 3 weeks oral supplementation of their current oral AAP. Data on adverse events(AEs), vital signs and movement disorder scales and on maintenance of effect was collected.

Results: The interim safety analysis set consists of 22 subjects on LAIR and 16 on oral AAP (olanzapine=2, quetiapine =7, risperidone = 6). Mean treatment duration(days) for LAIR and oral AAP was: 98 (SD 56) and 152 (SD 43) respectively. Mean change in BARS was -.2 (SD1.1) for LAIR and .3(SD.3), AIMS: -.3 (SD1.4) and .7 (SD3.4); SAS: .1 (SD1.4) and -.3(SD.8) respectively. Mean weight loss of -.3 kg on LAIR and mean gain of .3 kg on oral AAP.17/22 LAIR subjects and 14/15 (1 subject had no adverse event data available) AAP subjects reported AEs. Most common AEs in the LAIR group: headache 18%, nausea 14%, fatigue 14%, hyperkinesias 9%; and in the AAP group: flu-like symptoms 33%, somnolence and vomiting 20% each; nausea, dizziness, anxiety, 13% each; hyperkinesias 7%. Baseline mean CGI-S for both arms was 3.3 with a

-.3(SD1.7)and -.7(SD1.0) improvement for LAIR and AAP respectively.

Conclusion: These preliminary interim data suggest low propensity for movement disorders in subjects on LAI risperidone and similar adverse events for both groups. Maintenance of treatment effect was similar in both groups.

References:

1. Prien RF, Potter WZ. NIMH workshop report on treatment of bipolar disorder. Psychopharmacol Bull 1990;26:409-27.
2. Tohen M, Keter TA, Zarate CA, Suppes T, Frye M, Altshuler L, Zajecka J, Schuh, LM, Risser RC, Brown, E, Baker RW. Olanzapine versus divalproex sodium for the treatment of acute mania and maintenance of remission: a 47-week study. Am J Psychiatry 200.

NR211 Monday, May 22, 3:00 PM - 5:00 PM

The Relationship Between Early Changes in the HAMD-17 Anxiety/Somatization Factor Item of Somatic Symptoms (Gastrointestinal) and Antidepressant Treatment Outcome

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Schwartz, M.S.C., Eden A. Evins, Christina M. Dording, Maurizio Fava

Educational Objectives:

At the conclusion of this presentation, teh participant should be able to demonstrate knowledge of the relationship between somatic symptoms and depression.

Summary:

Objective: The 17-item Hamilton Rating Scale for Depression (HAMD-17) Anxiety/Somatization factor includes six items: Anxiety (psychic), Anxiety (somatic), Somatic Symptoms (gastrointestinal), Somatic Symptoms (general), Hypochondriasis, and Insight. This study examines the relationship between early changes (defined as those observed between baseline and week 1) in these HAMD-17 Anxiety/Somatization Factor items and treatment outcome among MDD patients participating in a 12-week study of fluoxetine.

Method: Five hundred and seventy patients with MDD diagnosed by the Structured Clinical Interview for DSM-IV (SCID) were given 12 weeks of fluoxetine with flexible dosing [target dosages: 10 mg daily (week 1), 20 mg daily (weeks 2-4), 40 mg daily (weeks 4-8), and 60 mg daily (weeks 5-12)]. The relationships between early changes in HAMD-17 anxiety/somatization factor items and treatment outcomes were assessed by logistic regressions that included baseline HAMD-17 scores as a covariate.

Results: Adjusting for baseline HAMD-17 scores, patients who remitted (HAMD-17 score <8) after study treatment had experienced significantly greater early improvement in Somatic Symptoms (Gastrointestinal) scores than non-remitters ($\chi^2(1)=8.29$; p= 0.004). Early changes in the remaining items were not significantly different between remitters and non-remitters.

Conclusion: In an earlier study by our group, the presence of early improvement on the HAMD-17 item concerning fatigue and general somatic symptoms was significantly predictive of achieving remission at endpoint with active study treatment. These results were not duplicated in the current study, as only early changes in somatic symptoms (gastrointestinal) were predictive of remission. Early changes in somatic symptoms (GI) may be linked to antidepressant treatment outcome, which is consistent with studies suggesting a relationship between somatic symptoms and depression.

References:

1. Nierenberg AA, Farabaugh AH, Alpert JE, Gordon J, Worthington JJ, Rosenbaum JF, Fava M. Timing of onset of antidepressant response with fluoxetine treatment. Am J Psychiatry 2000; 157:1423-1428.
2. Szegedi A, Muller MJ, Anghelescu I, Klawe C, Kohnen R, Benkert O. Early improvement under mirtazapine and paroxetine predicts later stable response and remission with high sensitivity in patients with major depression 2003; 64: 413-420.

NR212 Monday, May 22, 3:00 PM - 5:00 PM

The Self Report Form for Mood Episodes in Bipolar Disorder

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Educational Objectives:

At the conclusion of this session, the participant should be able to assess the value of bipolar patient reported mood symptoms as a reflection of DSM-IV bipolar mood states using a Self Report Form..

Summary:

Aim: To compare the Self Report Form for Mood Episodes (SRF-ME) to clinician ratings to determine mood states in bipolar patients.

Methods: 100 randomly selected patient records were examined which included both a completed Sustained Release F-ME and the prospectively assigned diagnosis by the treating clinician. Treating Clinician diagnosis was obtained from the standardized Clinical Monitoring Form (CMF), which includes a version of the SCID current mood modules modified to allow expanded symptom severity scoring. At the time of diagnosis, the treating clinician had access to the Sustained Release F-ME. The Sustained Release F-ME includes self-reported frequency of 13 DSM-IV symptoms of mood elevation and depression. The Sustained Release F-ME was administered in the clinic waiting room prior to routine clinical visits. For this chart review, the Sustained Release F-ME diagnosis was made a blinded clinician (GS) applying DSM-IV criteria to the form. Sensitivity and specificity were determined for full syndromal mood states 'depression,' 'mania,' 'mixed,' 'subsyndromal' states, and 'recovered.'

Results: Overall agreement between rater on the Sustained Release F-ME and CMF was 73%.

Sensitivity, Specificity, PPV, NPV
Mania/hypomania: 0.83, 0.97, 0.80, 0.98
Mixed: 0.77, 1.0, 1.00, 0.97
Depression: 0.71, 0.92, 0.77, 0.91
Recovered: 1.00, 0.75, 1.00, 0.53
Subsyndromal: 0.55, 0.94, 0.80, 0.82
PPV- Positive Predictive Value, NPV- Negative Predictive Value

For individual symptoms, discordance between CMF and Sustained Release F-ME ratings was greatest for impaired concentration (32%), self esteem (28%) and distractibility (27%); and least for suicidal ideation (7%) and risk taking (8%).

Conclusion: The Sustained Release F-ME demonstrated excellent sensitivity and specificity for hypomania and mania as well as for depression, but the treating clinician rated several symptoms differently than the patient. Overall, the Sustained Release F-ME appears to be an acceptable tool to detect DSM-IV defined mood states in bipolar patients.

References:

1. Sachs, G. S., Thase, M. E., Otto, M. W., Bauer, M., Miklowitz, D., & Wisniewski, S. R. et al.: Rationale, design, and methods of the systematic treatment enhancement program for bipolar disorder (STEP-BD). Biological Psychiatry 2003; 53(11): 1028-104.
2. Hirschfeld, R.M., Cass, A.R., Holt, D.C., Carlson, C.A. Screening for bipolar disorder in patients treated for depression in a family medicine clinic. J Am Board Fam Prac 2005; 18(4): 233-9.

NR213 Monday, May 22, 3:00 PM - 5:00 PM

Long-Term Effects of Aripiprazole on the Lipid Profiles of Patients With Bipolar I Disorder

Aneta Fornal, Pharm.D. *Bristol-Myers Squibb Company, 777 Scudders Mill Road, Plainsboro, NJ, 08536*, Linda Rollin, Ph.D., Margaretta Nyilas, M.D., Frederick Grossman, D.O., Andrei Pikalov, M.D., Raymond Sanchez, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to list the detrimental changes in lipid levels that can occur with the use of certain antipsychotic medications for bipolar mania. They should also be able to appreciate that treatment of bipolar mania with aripiprazole is not associated with abnormal lipid levels, as demonstrated by analysis of a placebo-controlled long-term trial for bipolar I disorder.

Summary:

Objective: Assess serum lipid level changes in patients with bipolar I disorder initially stabilized on open-label aripiprazole for ≥6 weeks, then randomized to placebo or aripiprazole (15mg/d or 30mg/d) for a 6-month maintenance phase. These patients subsequently entered a double-blind, 17-month extension phase. These analyses were requested by the FDA.

Methods: Incidences of treatment-emergent abnormal lipid levels associated with aripiprazole 15-30mg/d (n=77) or placebo (n= 83) were assessed at Weeks 8, 16, 26, 38, 52, 76, and 100. Statistical differences were compared using the Fisher's Exact Test. The FDA requested that thresholds for abnormal lipid values be based on guidelines from the NCEP ATP III. Abnormal lipid values were defined as total cholesterol ≥240mg/dL, low-density lipoprotein (LDL) ≥160mg/dL, high-density lipoprotein (HDL) <40mg/dL, or triglycerides ≥200mg/dL. Mean changes (baseline to endpoint) in lipid levels were analyzed by ANCOVA.

Results: Total pooled incidences of abnormal fasting and nonfasting lipid levels did not differ significantly between aripiprazole- and placebo-treated patients: total cholesterol = 11/74(14.9%) aripiprazole, 11/73(15.1%) placebo; LDL = 10/74(13.5%) aripiprazole, 9/73(12.3%) placebo; HDL = 33/74(44.6%) aripiprazole, 24/73(32.9%) placebo; triglycerides = 26/74(35.1%) aripiprazole, 25/73(34.2%) placebo. Mean changes (baseline to endpoint) in lipid levels were also not significantly different between aripiprazole- and placebo-treated patients: total cholesterol (mean [SE]) = 5.0mg/dL (4.0) aripiprazole, 0.6mg/dL (3.4)placebo; LDL = 5.4mg/dL (3.3)aripiprazole, 3.5mg/dL (2.7)placebo; HDL = 2.1mg/dL (1.0)aripiprazole, -0.2mg/dL (1.2) placebo; triglycerides = -23.4mg/dL (12.4) aripiprazole, -17.2mg/dL (8.9) placebo. When patients were divided into fasting and nonfasting groups, incidences of abnormal lipid levels and mean changes (baseline to endpoint) in lipid levels remained non-significant between aripiprazole and placebo.

Conclusion: Lipid profiles in long-term aripiprazole treatment of patients with bipolar I disorder were comparable to placebo.

References:

1. Koro CE, Fedder DO, L'Italien GJ, et al: An assessment of the independent effects of olanzapine and risperidone exposure on the risk of hyperlipidemia in schizophrenic patients. Arch Gen Psychiatry 2002; 59:1021-1026.

2. National Institutes of Health: Third Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Adult Treatment Panel III. Bethesda, MD, National Institutes of Health.

NR214 Monday, May 22, 3:00 PM - 5:00 PM

Predictors of Psychiatric Inpatients' Level of Depression at Discharge

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Educational Objectives:

1. Provide data on BDI scores for psychiatric inpatients on a Cognitive Therapy Unit.
2. Explicate gender differences on the BDI
3. Analyze predictors of level of depression at discharge from an inpatient Cogntive Therapy Unit
4. Offer interpretations and recommendations based on the data

Summary:

Objective: This was a third study in a three part project examining BDI scores in psychiatric patients hospitalized on a Cognitive Therapy Unit. More specifically, the study examined the predictors of depression at discharge in psychiatric inpatients. Method: Data on 187 predominantly Caucasian psychiatric inpatients were collected in the first six months of 1994. BDI and scores on a social perceptioin measure designed for this study were culled from the patients charts along with demographic information and information on length of stay (LOS). Participants with incomplete data were excluded from the analyses. Results:As hypothesized, statistically significant gender differences were found on the BDI (t= 2.49, df=107, p,.01) at both admission and discharge (t=.2.58, 107, p,.01). Missing data created a fan-shaped variance pattern for a plot of residuals indicating that the variance was not equal for all levels of the predictor variables. Therefore, a weighted least square regression analysis was employed to test which variables best predicted discharge depression. Depression at admission, gender, and length of stay powerfully predicted depression at dicharge accounting for 41 % of the variance in discharge depression scores. (R Square=.41, df=67, p<.001). Admission BDI scores were the most powerful predictors explaining 23 % of the variance with length of stay accounting for 11%, and gender contributing to 7% of the variance. The scores on the social perception measure did not significantly contribute to the regression equation. Conclusions: Female inpatients reported more depressive symptoms at both admission and discharge than their male counterparts. Having more severe depression at admission, being female, and being hospitalized for a greater length of time predicted depression at discharge. Discussion: Several factors may account for the gender differences on the BDI scores. First, since scores for hospitalized men were lower at admission, there may be a lower threshold for hospitalization for depressed men. Males may be more likely to be hospitalized with less self-reported symptoms than women. Accordingly, women may have to report higher levels of distress in order to receive appropriate care. It may also be more socially appropriate for women to report depressive symptoms than it is for males to report symptoms. There are also several possible explanations for the results of the regression analysis. A hospital stay itself may represent a stressor for patients thereby increasing their level of depression. Separation from significant others may result in a loss of reinforcement and subsequently increase depressive symptoms. For others, discharge may represent a return to pernicious and stessful living environments which contribute to increased depression. Therefore, brief therapeutic hospitalizations which not only focus on individual symptoms but also include a family/interpersonal relationship component may be effective.

References:

1. Friedberg, RD et al:Perceptions of treatment helpfulness and depressive symptomology in psychiatric inpatients on a cognitive therapy unit. J of Rational Emotive and Cognitive Behavioral Therapy, 1999, 17, 33-50.

2. Hammen C, & Garber, J: Vulnerability to depression across the lifespan. In Vulnerability to psychopathology, edited by Ingram, RE & Price, JM, New York, Guilford Press, pp. 258-270.

NR215 Monday, May 22, 3:00 PM - 5:00 PM

Clinical Correlates Associated With Antidepressant-Related Mania

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Willem A. Nolen, M.D., Trisha Suppes, M.D., Heinz C. Grunze, M.D., Robert M. Post, M.D.

Educational Objectives:

Educational Objectives **At the conclusion of this presentation, the participant will have an appreciation of clinical correlates that are associated with treatment-emergent mania in bipolar depressed patients.**

Summary:

Introduction

Antidepressant -related mania (ADrM) is a common clinical concern that can have substantial negative impact on overall mood stability in bipolar patients.

Method

This post-hoc study examined the clinical correlates associated with ADrM during a 10-week, randomized, double-blind comparison of sertraline, bupropion, and venlafaxine as adjuncts to mood stabilizers for patients with bipolar depression. Three groups were identified and defined as follows: 1.) ADrM- CGI manic severity score >/= 4 at any time during the trial; 2.) Antidepressant response (ADR) - CGI depression severity score </= 3ill; 3.) Antidepressant non-response (ADNR) - CGI change from preceding phase for depression >/= 3.

The trial summary was used to identify any demographic or clinical differences between the 3 groups. A second analysis evaluated any baseline symptom severity rating (Inventory for Depression Symptoms or IDS, Young Mania Rating Scale or YMRS) differences between the 3 groups. As the latter data had a non-normal distribution, the ANOVA and post hoc t-tests were confirmed with general linear modeling based on a Poisson process.

Results

There were no significant demographic or clinical differences in the ADrM (n=48), ADR (n=94), and ADNR (n=50) groups. Baseline manic symptoms as measured by the YMRS were significantly different between groups (ADrM = 3.8 +/- 4.9; ADR= 1.9 +/- 2.5; ADNR= 2.4 +/- 2.5; F(2,187) = 5.33, p= 0.006). The individual YMRS items that were significantly higher in the ADrM versus ADR/ADNR groups were motor activity, speech, and thought content. The overall YMRS and these individual items remained significantly different among the 3 groups after poisson linear modeling and bonferroni correction.

Conclusions

These data suggest baseline subjective symptoms of heightened motor activity, talkativeness, and new interests are associated with an antidepressant-related manic episode. A careful examination for manic like symptomatology is warranted prior to antidepressant treatment for patients with bipolar depression.

References:

1. 1. Frye MA, Gitlin MJ, Altshuler LL. Unmet needs in bipolar depression. Depress Anxiety 2004; 19(4): 199-208.
2. 2. Keck PE, Corya SA, Altshuler LL, Ketter TA, McElroy SL,and Tohen M. Analyses of treatment-emergent mania with olanzapine/fluoxetine combination in the treatment of bipolar depression. J Clin Psychiatry 2005 66: 611-6.

NR216 Monday, May 22, 3:00 PM - 5:00 PM

Predictors of Legal Involvement in Patients With Dual Diagnosis, Rapid Cycling Bipolar Disorder

Stephen J. Ganocy, Ph.D. *Case Western Reserve University, School of Medicine, 11400 Euclid Ave. Suite 200, Cleveland, OH, 44106*, Joseph R. Calabrese, M.D., Omar Elhaj, M.D., Keming Gao, M.D., Sarah Bilali, M.A., Carla Conroy, B.A.

Educational Objectives:

Determine what factors lead to legal complications in a cohort of patients with a substance use disorder (SUD) and rapid cycling bipolar disorder (RCBD).

Summary:

Methods:

Patients enrolled into ongoing clinical trials meeting DSM-IV criteria for RCBD and SUD were administered the legal section of the Addiction Severity Index (ASI) (McLellan et al 1980 and 1983)

Results:

172 research participants were valid candidates for the analysis. Logistic regression was employed to determine how many of 16 candidate explanatory variables could be used as predictors for the presence/absence of legal involvement. Forty observations were excluded from the analysis due to having a missing value in at least one of the 16 candidate variables, or in the response variable. Thus the total number of cases used in the final analysis was 132. The number with legal involvement was 82 out of 132. Of the candidate explanatory variables only 5 were found to be statistically significant predictors of legal involvement. The odds ratios for the 5 significant predictors were (1) Gender (Male versus Female), 2.76 (95% CI: 1.25, 6.13), (2) Any Anxiety (No versus Yes), 3.54 (1.40, 8.91), (3) Number of Lifetime SUD's (>1 versus < 1), 3.13 (1.35, 7.18), (4) Psychotic Symptoms (Yes versus No), 2.49 (1.10, 5.65) and (5) Time to Treatment for Mania, 1.04 (1.00, 1.08). The greatest risk for having legal involvement then occurred in: Males, no anxiety, number of lifetime SUD's > 1 with psychotic symptoms and longer times to treatment for mania.

Conclusion:

The significant predictors to legal involvement include gender, lack of anxiety, number of lifetime SUDs, presence of psychotic symptoms and the length of time to receiving an accurate diagnosis of bipolar disorder. These results highlight the need to explore further the clinical relevance of comorbidity to legal complications, as well as the need for early detection of the diagnosis.

References:

1. McLellan AT, Luborsky LL, Woody GE et al: Predicting response to alcohol and drug abuse treatments. Arch Gen Psychiatry 1983;620-625.
2. McLellan AT, Luborsky LL, Woody GE, O'Brien CP: An improved diagnostic evaluation instrument for substance abuse patients. J Nerv Mental Disease. 1980;168:26-33.

NR217 Monday, May 22, 3:00 PM - 5:00 PM

Clinical Impacts of Comorbid Anxiety Disorder and Substance Use Disorder on Patients With Rapid Cycling Bipolar Disorder

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Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the clinical impacts of comorbid anxiety disorder and substance use disorder in patients with rapid cycling bipolar I or II disorder.

Summary:

Objective: To investigate the clinical impacts of comorbid anxiety disorder (AD) and substance use disorder (SUD) in patients with rapid cycling bipolar disorder (RCBD).

Methods: Data of patients with RCBD who enrolled in our research studies were analyzed for the impacts of AD including GAD, panic disorder (PD), and OCD and SUD, dependence or

abuse on demographic and clinical presentations. Diagnoses were ascertained by using the Mini International Neuropsychiatric Interview at the initial assessment.

Results: Of 564 patients with RCBD, 261 of them (46%) had a lifetime history of AD and 371 (66%) had a lifetime history of SUD. Male patients had a significantly higher rate of SUD than female patients (55% versus 45%), but they had an insignificantly difference in the rates of AD (46% versus 54 %). Patients with BPI had significantly higher rates of AD (67% v. 48%) and SUD (63% versus 44%) compared with their BPII counterparts. Patients with a lifetime history of AD had significantly increased rates of psychosis (48% versus 37%) and hospitalization (60% versus 50%). Similarly, patients with a history of SUD had significantly increased rates of psychosis (49% versus 32%) and suicide attempt (44% versus 35%). There was also a trend increase in the rate of suicide attempt (44% versus 39%) in patients with lifetime AD.

Conclusion: Comorbid AD and SUD in patients with RCBD had negative impacts on the clinical presentations as reflected by increased rates of psychosis, hospitalization, and suicide attempt. Both conditions should be taken seriously during the clinical assessment and treatment.

References:

1. Simon NM, Otto MW, Wisniewski SR, et al. Anxiety disorder comorbidity in bipolar disorder patients: Data from the first 500 participants in the systematic treatment enhancement program for bipolar disorder (STEP-BD). Am J Psychiatry 2004; 161:2222-22.
2. Boylan KR, Bieling PJ, Marriott M, et al. Impact of comorbid anxiety disorders on outcome in a cohort of patients with bipolar disorder. J Clin Psychiatry 2004; 65:1106-1113.

NR218 Monday, May 22, 3:00 PM - 5:00 PM

Onset of Action of Quetiapine Monotherapy in Bipolar Mania

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to evaluate the onset of action of quetiapine monotherapy compared to placebo in adults with bipolar disorder.

Summary:

Background: Quetiapine monotherapy has been shown to be effective and well tolerated in bipolar mania.[1,2]

Objective: Evaluate the onset of action of quetiapine monotherapy in bipolar mania.

Methods: Two 12-week, randomized, placebo-controlled trials of quetiapine monotherapy[1,2] were examined to determine the time of first significant improvement in YMRS score for quetiapine relative to placebo in patients with DSM-IV bipolar I disorder experiencing a manic episode. The first evaluation in both studies was Day 4.

Results: A significant difference (P<0.01) between quetiapine and placebo in total YMRS score improvement was first noted by Day 4 in one monotherapy trial[1] and Day 7 in the other.[2] Pooling of data from the two studies indicated an onset of action by Day 4 (P=0.021). Analysis of YMRS items in the pooled dataset showed an onset of action for quetiapine in three items (appearance, speech rate/amount, and sexual interest) by Day 4 and in three further items (increased motor activity, sleep, and language/thought disorder) by Day 7 (P<0.05). Quetiapine improved all 11 YMRS items significantly by Day 21, with maintenance of these improvements to study end (Day 84). Adverse events by Day 4 (during quetiapine dose escalation) included somnolence, dry mouth, and insomnia.

Conclusions: Quetiapine monotherapy is effective and generally well tolerated in patients with bipolar mania, with an onset of action as early as Day 4.

Supported by funding from AstraZeneca Pharmaceuticals LP.

References:

1. McIntyre RS, Brecher M, Paulsson B, Huizar K, Mullen J. Quetiapine or haloperidol as monotherapy for bipolar mania-a 12-week, double-blind, randomised, parallel-group, placebo-controlled trial. Eur Neuropsychopharmacol 2005;15(5):573-85.
2. Bowden CL, Grunze H, Mullen J, Brecher M, Paulsson B, Jones M, et al. A randomized, double-blind, placebo-controlled efficacy and safety study of quetiapine or lithium as monotherapy for mania in bipolar disorder. J Clin Psychiatry 2005;66(1):111-21.

NR219 Monday, May 22, 3:00 PM - 5:00 PM

Lamotrigine for Acute Treatment of Bipolar Depression: A Retrospective Pooled Analysis of Response Rates in Three Randomized Trials

John Geddes *University of Oxford, Warneford, University of Oxford, Warneford Hospital, Oxford, OX3 7JX, United Kingdom*, Andrew Nierenberg, Eric Bourne, Bryan Adams, Robin White, Kevin Nanry, Robert Leadbetter

Educational Objectives:

At the conclusion of this presentation, the participant should be able understand patient response and tolerability to lamotrigine treatment.

Summary:

Objective: Bipolar depression is a significant burden for patients and there is a need to improve methods used in clinical trials to identify effective treatments.[1,2] A retrospective combined analysis of responder rates in three randomized, double-blind, placebo-controlled trials of lamotrigine for the acute treatment of bipolar depression is discussed.

Methods: Data were pooled from three randomized trials that included 579 participants with bipolar I or II disorder and who had a major depressive episode. Efficacy was evaluated weekly with the Montgomery-Asberg Depression Rating Scale (MADRS). The percentage of patients that achieved a ≥50% or a ≥75% improvement on the MADRS from baseline, and full remission of symptoms (MADRS ≤10 observed on 2 consecutive assessments) were compared between the lamotrigine and placebo groups by week. Since the studies were not equal in length, data were truncated to the shortest duration of the three studies (7 weeks). Analysis of covariance was conduced using a last observation carried forward (LOCF) approach.

Results: More patients treated with lamotrigine than placebo achieved a ≥50% improvement from baseline at weeks 5, 6, and 7 with 49% versus 35% (p=0.003), 56% versus 43% (p=0.007), and 64 % versus 45% (p<0.001) responders, respectively. At week 7, more patients who received lamotrigine than placebo achieved a ≥75% or greater improvement from baseline (39% versus 19% responders, p<0.001) and full remission of symptoms (38% versus 27%, p=0.025).

Conclusion: Lamotrigine was superior to placebo in response and remission outcomes for the treatment of acute depression over 7-weeks in patients with bipolar disorder.

This study was supported by GlaxoSmithKline.

References:

1. Judd LL and Akiskal HS. Depressive episodes and symptoms dominate the longitudinal course of bipolar disorder. Curr Psychiatry Rep. 2003; 6:417-8.

2. Muzina MJ and Calabrese JR. Recent placebo-controlled acute trials in bipolar depression: focus on methodology. International Journal of Neuropsychopharmacology. 2003; 6: 285'291.

NR220 Monday, May 22, 3:00 PM - 5:00 PM

Effectiveness of Escitalopram Versus Venlafaxine XR in Major Depression in a Real World Clinical Setting

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Educational Objectives:

At the conclusion of this presentation, the participants should be able to compare the effectiveness of escitalopram versus venlafaxine XR in Major depression (MDD) in the real world clinical setting.

Summary:

Objective: To compare the effectiveness of escitalopram versus venlafaxine XR in Major depression (MDD) in the real world clinical setting.

Methods: The clinical research information system (CRIS) is the electronic medical record of all patients seen in Psychiatry at the Duke University Medical Center since 1998. The database includes 25,632 patients and 119, 086 patient-visits. All patients meeting criteria for MDD, started for the first time on escitalopram (245) or venlafaxine XR (415) and seen for at least two visits were analyzed. Efficacy (measured by CGI), tolerability demographics, dosing, comorbidity and severity of MDD (DSM-IV criteria) were analyzed. CGI of 1 was considered remission.

Results; Patients started on escitalopram were more likely to be African-American and have more severe depression (escitalopram=29,4% versus venlafaxine XR=26.7%) (χ^2=12.1, p=0.015). There were no differences in comorbidity of anxiety disorders in the 2 groups. The mean duration of treatment was longer in the venlafaxine XR group (276±348 days) compared to the escitalopram group (136±184 days) which may reflect the later introduction of escitalopram. There were no differences in the rates of remission on escitalopram (22%) versus venlafaxine XR (27%) (χ^2=2.22, p=0.32). The time to remission was significantly shorter in the escitalopram group (116±135 days) compared to the venlafaxine XR (142±149 days) group (F=21.66, p<0.0001).

Conclusions: Escitalopram and venlafaxine XR were equally likely to lead to remission of MDD despite patients started on escitalopram being more depressed at baseline. It appears that treatment with escitalopram achieves remission earlier than venlafaxine XR.

References:

1. Sir A, D'Souza RF, Uguz S, George T, Vahip S, Hopwood M, Martin AJ, Lam W, Burt T: Randomized Trial of Sertraline Versus Venlafaxine XR in Major Depression: Efficacy and Discontinuation Symptoms. J Clin Psychiatry 2005; 66:1312-1320.

2. Murdoch D, Keam SJ: Escitalopram: A Review of its use in the Management of Major Depressive Disorder. Drugs. 2005; 65:2379-2404.

NR221 Monday, May 22, 3:00 PM - 5:00 PM

Impact of Galantamine on Cognition in Bipolar Disorder

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to determine if galantamine augmentation improves cognition in euthymic bipolar patients.

Summary:

Background: There is increasing evidence that cognitive impairment is common in patients with bipolar disorder. While Galantamine has been shown to improve cognitive function in Alzheimer's disease, it has not yet been studied in other psychiatric populations. This is the first double blind randomized clinical trial of galantamine for cognitive impairment in bipolar disorder.

Method: A double-blind placebo, cross-over controlled 24-week study was conducted in euthymic bipolar outpatients (types I, II, or NOS) with subjective reports of cognitive complaints. A neuropsychological test battery was administered at study entrance, three months, and six months. Tests administered included Delis-Kaplan Executive Function System D-KEFS subtests: Trails Making Test and Verbal Fluency Test, California Verbal Learning Test-II, Wisconsin Card Sorting Test (WCST), and Boston Naming Test. The Wechsler Abbreviated Scale of Intelligence (WASI) was administered at study entry only to assess intelligence.

Results: Before breaking the blind, improvement in cognitive function was observed in the majority of the sample. After breaking the blind, full data on 30 patients will be presented.

Conclusions: The impact of galantamine on cognition of euthymic bipolar patients will be discussed.

Funding Source: Janssen/Ortho-McNeil (Reminyl IIS)

References:

1. Zubieta, JK, Huguelet, P, O'Neil, RL, Giordani, BJ. Cognitive function in euthymic bipolar I disorder.

2. Raskind MA, Peskind ER, Wessel T, Yuan W. Galantamine in AD: A 6-month randomized, placebo-.

NR222 Monday, May 22, 3:00 PM - 5:00 PM

A Single-Blind Evaluation of Divalproex Sodium Versus Olanzapine for Alcohol Use Relapse Prevention in Bipolar Disorder

Michael Gitlin, M.D. *UCLA, Psychiatry, 300 UCLA Medical Plaza, Suite 2437, Los Angeles, CA*, Mark A. Frye, M.D., Jason W. Chirichigno, M.A., James McKowen, B.S., Jim Mintz, Ph.D., Eric M. Levander, M.D., Lori Altshuler, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant will have an appreciation of the impact of mood stabilization treatment on alcohol related outcome measures in patients with bipolar disorder.

Summary:

Introduction

Little research has been done to evaluate the effectiveness of mood stabilizers in bipolar patients who are actively drinking.

Methods

This 52-week, single-blind randomization evaluated the effectiveness of divaproex sodium (DVPX) versus olanzapine (OLZ) in actively drinking bipolar outpatients. After obtaining written in-

formed consent, 50 subjects (31 men/ 19 women) were randomized. The primary outcome measure was a return to hazardous drinking [5 (men) or 4(women) drinks/day] and was measured using Kaplan-Meier survival curve methodology.

Results

14 subjects entered the study manic (mean YMRS 17.36 ÃƒÆ'Ã¢â'¬~Ãƒâ€~Ã'Â± 4.94; mean DVPX serum level = 89.3 +/- 14.8 mcg/dl; mean OLZ dose = 7.5 +/- 5.5mg). 36 subjects entered the study depressed (mean IDS 33.0 ÃƒÆ'Ã¢â'¬~Ãƒâ€~Ã'Â± 8.4; mean DVPX serum level = 67.3 +/- 34.7 mcg/dl: mean OLZ dose at final visit = 5.3 +/- 2.4 mg).

Of the 50 subjects who were randomized, 25 [16M/9W; DVPX = 11 (8M/3W); OLZ =14 (8M/6W)] dropped due to a return of hazardous drinking. By survival curve analysis, there was a trend difference in survival between DVPX (n=11, 50% median =174 days [95% CI: 32 days - NC]) and OLZ (n=14, 50% median =73 days [95% CI: 29-86 days]; log-rank Chi-square = 3.19, df=1,p=0.07).

For men, there was no difference in survival between DVPX and OLZ. For bipolar women, there was a significant difference in survival between DVPX (n=3, median survival could not be estimated as > 50% remained at risk at the end of the trial) and OLZ (n=6, 50% median =52 days [95% CI: 8-109 days]; log-rank Chi-square = 5.07, df=1, p=0.02).

Conclusion

This study is limited by its small sample size and lack of randomized blind. Nonetheless, it suggests a differential rate of relapse to alcoholism in bipolar women on DVPX versus OLZ. Further work is encouraged to confirm these preliminary data.

References:

1. Frye MA, Altshuler LL, McElroy SL, et al. Gender differences in prevalence, risk and clinical correlates of alcoholism comorbidity in Bipolar Disorder. Am J Psychiatry. May 2003; 160 (5): 883-889.
2. Salloum IMC, Daley DC, Kirisci L, Himmelhoch J, Thase ME. Efficacy of valproate maintenance in patients with bipolar disorder and alcoholism: a double-blind placebo controlled study. Arch Gen Psychiatr. 2005;62(1):37-45.

NR223 Monday, May 22, 3:00 PM - 5:00 PM

Quality of Life and Cognitive Function: Results From a Large, 12-Week Controlled, Open-Label Study of Dermatologic Precautions With Lamotrigine in the Treatment of Adults and Adolescents With Bipolar I Disorder

Jay Graham *GlaxoSmithKline, 5 Moore Drive, RTP, NC, 27709-3398*, Steven Burch, Jeremy Roberts, Thomas Thompson

Educational Objectives:

At the conclusion of this presentation, the participant should be able understand patient response and tolerability to lamotrigine treatment.

Summary:

Objective: Bipolar disorder and medications used in its treatment are associated with cognitive impairment[1]. The effect of lamotrigine on cognition and quality of life was assessed as secondary endpoints in a large outpatient study[2] measuring the affect of administering specific dermatological precautions on overall rash rates with lamotrigine.

Methods: Adult and adolescent patients (≥13 years old) were administered open-label lamotrigine titrated to a target dosage of 200 mg/day, adjusting for concomitant bipolar medications, and continued for 12 weeks. Patients were administered self-reported Quality of Life and Enjoyment and Satisfaction Questionnaire Short Form (Q-LES-Q-SF) and Medical Outcomes Study Cognition Scale (MOS-Cog) via interactive voice response system (IVRS) at baseline and end of study (Week 12). Analyses were performed using a last observation carried forward (LOCF) approach.

Results: 188 sites enrolled 1139 patients as the intent-to-treat population. Mean scores from general activities of life enjoyment questions from the Q-LES-Q-SF and the MOS-Gog improved during the 12 weeks of adjunctive treatment with a change from baseline score of 10.1 (n=914, SD 20.07, p<0.0001) and 8.4 (n= 912, SD 22.55, p<0.0001), respectively. No serious rash was reported.

Conclusions: In a large outpatient study, self-reported quality of life enjoyment and cognitive function scores improved over 12 weeks when lamotrigine was added to current bipolar therapy.

This study was supported by GlaxoSmithKline.

References:

1. Meador KJ. Newer anticonvulsants: dosing strategies and cognition in treating patients with mood disorders and epilepsy. J Clin Psychiatry. 2003; 64 Suppl 8:30-4.
2. Ketter TA et al. The Effect of Dermatologic Precautions on the Incidence of Rash with Addition of Lamotrigine in the Treatment of Bipolar I Disorder. J Clin Psych. In Press.

NR224 Monday, May 22, 3:00 PM - 5:00 PM

The Prevalance and Construct of Anger Attacks in Depressive and Other Neurotic, Stress Related, and Somatoform Disorders

Nitesh Prakash Painuly, M.D. *Chandigarh*, Sandeep Grover, M.D., Nitin Gupta, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to [1] demonstrate the high prevalence and importance of recognizing anger attacks in patients with depression, neurotic, and other stress related disorders, and [2] suggest that anger attacks need to be conceptualized as a distinct syndrome (i.e.'anger disorder') on similar conceptual lines as existing for panic disorder.

Summary:

Objective: Anger attacks are episodes of intense anger with a crescendo of autonomic arousal that occur in response to trivial provocation and lead to intense guilt afterwards. Till date, anger attacks have been mostly studied in depression. The main objectives of the study were to [1] determine the prevalence of AA in neurotic psychiatric disorders (including non-psychotic depression and anxiety disorders), and [2] explore the possibility of AA being a distinct syndrome.

Methods: The sample comprised 328 patients. This was divided into two groups: patients with anger attacks (n=170), and patients without anger attacks (n=158); presence of anger attacks being determined using the Anger Attack Questionnaire. Psychiatric diagnoses were based on ICD-10. Both groups were administered socio-demographic and clinical profile sheet, Irritability Depression Anxiety Scale and World Health Organization Quality of Life-BREF Version.

Results: 170 of the 328 subjects fulfilled the criteria for anger attacks giving a prevalence rate of 51.8%. The diagnosis of anger attacks was markedly prevalent across the various diagnostic categories, ranging from 35.29 % to 73.33 %. Nearly 69% of subjects suffering with comorbid anxiety and depressive disorders had AA. Patients with anger attacks exhibited more anxiety, irritability, and had poorer quality of life. Frequency of anger attacks was positively correlated with depression, irritability and aggression, and negative correlation was found with education, income and quality of life. Panic attacks, somatic anxiety and psychologi-

cal domain of quality of life predicted the categorization of subjects into with and without anger attacks.

Conclusion: **Anger attacks are frequent phenomena with a great degree of negative impact and tend to cut across various psychiatric disorders. There may be merit in conceptualizing anger attacks as a distinct syndrome on similar lines as existing for panic disorder.**

References:

1. Fava M, Anderson K, Rosenbaum JF. "Anger attacks": possible variants of panic and major depressive disorders. Am J Psychiatry 1990; 147: 867-870.

2. Fava M, Rosenbaum JF. Anger attacks in patients with depression. J Clin Psychiatry 1999; 60 (Suppl 15): 21-24.

NR225 Monday, May 22, 3:00 PM - 5:00 PM

Quality of Life in Patients With MDD

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Educational Objectives:

The quality of life is an appropriate measurement of outcome for many disorders including mental disorders. This study demonstrated the availability of the Korean WHOQOL-BREF, a short version of the WHOQOL-100, in patients with major depressive disorder.

Summary:

Objective : This study was designed to evaluate the quality of life (QOL) in patients with MDD according to the DSM-IV-TR classification of mood disorders using the brief form of World Health Organization Quality of Life (WHOQOL-BREF) instrument-Korean version.

Methods : Fifty patients with MDD were recruited from outpatient clinic and an informed consent was obtained from each of them. Hospital staff members volunteered as the control group. The 26 item WHOQOL-BREF instrument included questionnaires on the physical, psychological, social, and environmental domains and it was employed for testing the all subjects. The Hamilton Rating Scale for Depression (HAM-D) was applied for depressed patients.

Results : Physical (9.0 ± 1.9 versus 14.9 ± 2.6), psychological (8.7 ± 2.0 versus 13.0 ± 2.0), social (11.2 ± 2.7 versus 13.8 ± 2.3), and environmental domains (9.6 ± 1.8 versus 12.3 ± 2.1) were shown to have a worse quality of life for patients with MDD compared to normal control group irrespective of age difference ($p<0.001$). QOL in the patients with MDD were perceived as worsen based on its severity using HAM-D scores ($p<0.001$).

Conclusions : The individual subjective perception of their condition in patients with MDD should be regarded as an important factor. The physical, psychological, social, and environmental status of patients with MDD needs to be thoroughly thought over. In this context, the WHOQOL-BREF which reflects multi-dimensional state of well-being could be useful instrument for evaluating the outcome for MDD, adding to the objective assessment of function or severity of symptom in patients with MDD.

References:

1. The WHOQOL group: Development of the World Health Organization WHOQOL-BREF Quality of Life Assessment. Psychol Med 1998; 28:551-558.

2. Angermeyer MC, Holzinger A, Matschinger H, Stengler-Wenzke K: Depression and quality of life: results of a follow-up study. Int J Soc Psychiatry 2002; 48:189-199.

NR226 Monday, May 22, 3:00 PM - 5:00 PM

Quetiapine as Add-On Treatment for Bipolar I Disorder: Efficacy in Preventing Relapse of Depressive Episodes

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Educational Objectives:

At the conclusion of this session, the participants will be familiar with data on the efficacy of quetiapine combination therapy for the treatment of patients with bipolar I disorder who are inadequately responsive to standard medications.

Summary:

Objective: To assess the long-term response to add-on quetiapine therapy in patients with bipolar I disorder who were not adequately responding to standard medications.

Methods: Outpatients with bipolar I disorder (DSM-IV-TR) responding inadequately to standard treatment were observed before and after the addition of quetiapine. Symptom severity was evaluated using the Clinical Global Impression scale for bipolar disorder (CGI-BP) each month. Relapses included scores ≥1 point higher than previous CGI-BP scores and/or upward titration of quetiapine or other medications.

Results: 61 patients (age range of 18-68 years) were observed prospectively for an average of 7.5 months (range 3 to 18 months) prior to addition of quetiapine and subsequently followed for an average of 15.9 months (range 6 to 42 months).

The final mean quetiapine dose was 537.1±91.7 mg/day. Prior to quetiapine addition, an annual relapse rate of 2.09 episodes was recorded, relating to 0.94 depressive and 1.15 manic or mixed episodes. Following quetiapine addition, annual relapse rates were reduced to 0.62 episodes, representing 0.14 depressive and 0.46 manic or mixed episodes. Compared with the period of add-on quetiapine treatment, the relative risk of relapse *prior* to quetiapine therapy was 3.4 for all episodes ($\chi^2=24.8$, $P<0.001$), 6.7 for depressive episodes ($\chi^2=24.7$, $P<0.001$), and 2.5 for manic or mixed episodes ($\chi^2=9.0$, $P<0.001$).

Conclusions: This naturalistic follow-up study provides preliminary evidence for the efficacy of add-on quetiapine in the long-term treatment of manic or mixed and depressive episodes of bipolar I disorder, and particularly in the prevention of depressive episodes.

Supported by funding from AstraZeneca Pharmaceuticals LP.

References:

1. Carta MG, Angst J. Epidemiological and clinical aspects of bipolar disorders: controversies or a common need to redefine the aims and methodological aspects of surveys. Clin Pract Epidemol Ment Health 2005;1(1):4.

2. Calabrese JR, Keck PE, Jr., Macfadden W, Minkwitz M, Ketter TA, Weisler RH, et al. A randomized, double-blind, placebo-controlled trial of quetiapine in the treatment of bipolar I or II depression. Am J Psychiatry 2005;162(7):1351-60.

NR227 Monday, May 22, 3:00 PM - 5:00 PM

Quetiapine Monotherapy for Bipolar II Depression: Pooled Results From Two Placebo-Controlled Studies

Robert Hirschfeld *University of Texas Medical Branch, 301 University Boulevard 1.302RSH, Galveston, TX, 77555-0188*, Trisha Suppes, Eduard Vieta, Anders Carlsson, Göran Stening, Wayne Macfadden

Educational Objectives:

At the conclusion of this session, the participants will be able to evaluate the efficacy and safety of quetiapine in patients with depressive episodes of bipolar II disorder, an understudied population.

Summary:

Objective: To investigate the efficacy and tolerability of quetiapine monotherapy for depressive episodes in patients with bipolar II disorder.[1,2]

Methods: A post-hoc evaluation of 351 patients with bipolar II depression from two double-blind, randomized, placebo-controlled, 8-week studies of quetiapine (300 or 600 mg/d; once-daily, evening dosing) in patients with bipolar I or II disorder (DSM-IV) was conducted. The primary endpoint was change from baseline to Week 8 in MADRS total score (analyzed using mixed-effect model, repeated-measures). MADRS and HAM-D scores were assessed weekly.

Results: Improvement in mean MADRS total score from baseline (range 28.6-29.9 for the three groups) was significantly greater with quetiapine 300 and 600 mg/d from the first assessment (Week 1) through to Week 8. The change from baseline at Week 8 for quetiapine 300 and 600 mg/day and placebo was -17.09, -17.86, and -13.31 (P=0.005 and P=0.001 versus placebo), respectively. MADRS effect sizes for quetiapine 300 and 600 mg/d were 0.45 and 0.54, respectively. Improvements from baseline at Week 8 in mean HAM-D scores were also significantly greater with both quetiapine doses (-14.33, P=0.001, and -15.04, P<0.001) than placebo (-11.33). HAM-D effect sizes were 0.51 and 0.63 for quetiapine 300 and 600 mg/d, respectively. Common adverse events included dry mouth (300 mg/d: 48.3%; 600 mg/d: 43.1%; placebo: 13.7%), sedation (40.7%, 36.2%, 7.7%), and somnolence (20.3%, 19.0%, 6.0%). Adverse events were generally mild in intensity in both studies.

Conclusion: This analysis of two major randomized, controlled trials is, to our knowledge, the largest evaluation to date of an atypical as monotherapy for bipolar II depression. Quetiapine is one of the first agents to demonstrate significant efficacy as monotherapy, compared with placebo, for the treatment of depressive episodes in bipolar II disorder. Quetiapine was generally well tolerated in both studies.

Supported by funding from AstraZeneca Pharmaceuticals LP

References:

1. Keck PE, Jr., Nelson EB, McElroy SL. Advances in the pharmacologic treatment of bipolar depression. Biol Psychiatry 2003;53(8):671-9.

2. Calabrese JR, Keck PE, Jr., Macfadden W, Minkwitz M, Ketter TA, Weisler RH, et al. A randomized, double-blind, placebo-controlled trial of quetiapine in the treatment of bipolar I or II depression. Am J Psychiatry 2005;162(7):1351-60.

NR228 Monday, May 22, 3:00 PM - 5:00 PM

Efficacy of Duloxetine Versus Combined SSRIs (Fluoxetine, Paroxetine, Escitalopram) and Placebo in the Treatment of MDD

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Educational Objectives:

At the conclusion of this session, participants will be able to evaluate the relative efficacy of duloxetine compared with several SSRIs in the treatment of major depression.

Summary:

Objective: Compare the efficacy of duloxetine with an SSRI group (including fluoxetine, paroxetine, escitalopram) and placebo.

Method: Data were pooled from all studies in which duloxetine and SSRIs have been compared: 7 randomized, double-blind, fixed-dose, 8-week studies of duloxetine (N=1133) versus SSRI (N=689; fluoxetine, paroxetine, or escitalopram) versus placebo (N=641). All studies were conducted in patients diagnosed with MDD. Duloxetine doses were 40 mg/day (2 studies); 60 mg/day (1 study); 80 mg/day (4 studies); and 120 mg/day (4 studies). SSRI doses were 10 mg/day (escitalopram) and 20 mg/day (fluoxetine and paroxetine).

Results: Differential efficacy was observed on some depressive symptoms compared with the SSRIs studied. When considering the efficacy of duloxetine across the studied dose range of 40-120 mg/day, duloxetine was significantly superior to the combined SSRIs (fluoxetine, escitalopram, paroxetine) on the 17-item Hamilton Depression Rating Scale (HAMD17) total score (-9.16 v -8.50; p = .032). This significant difference arose from significantly greater efficacy of duloxetine on HAMD17 individual items. Specific HAMD17 items for which duloxetine was significantly superior to combined SSRIs included work and activities, psychomotor retardation, sexual functioning, and hypochondriasis. Although there were no items for which the combined SSRI group was significantly superior to duloxetine, differences approached significance for middle insomnia (p = .057) and late insomnia (p = .06). The advantage of duloxetine over the combined SSRI group approached significance for the general somatic symptom item (p = .056).

Conclusion: This analysis of 7 pooled studies comparing duloxetine to the SSRIs fluoxetine, paroxetine, and escitalopram showed statistically significant advantage on the HAMD17 total score for duloxetine compared with the combined SSRIs. The differential efficacy was driven by greater improvement for duloxetine-treated patients on specific depressive symptoms of work and activities (anhedonia), psychomotor retardation, sexual functioning, and hypochondriasis. Funded by Eli Lilly and Company.

References:

1. Hirschfeld, R.M.A., Mallinckrodt, C, Lee, T.C., Detke, M.J. (2005). Time course of depression-symptom improvement during treatment with duloxetine. Depression and Anxiety, 21,170-177.

2. Mallinckrodt, C.H., Prakash, A., Andorn, A.C., Watkin, J.G., Wohlreich, M.M. (2005). Duloxetine for the treatment of major depressive disorder: A closer look at efficacy and safety data across the approved dose range. J of Psych Research, in press.

NR229 Monday, May 22, 3:00 PM - 5:00 PM

Assessment of the Impact of Atomoxetine on Fatigue and Executive Dysfunction Associated With MDD

M.Z. Hussain, M.D. *Prince Albert Mental Health Center, Psychiatry, 2727 2nd Avenue West, Prince Albert, AB, t2n1t1, Canada*, Seema Hussain, M.D., Waqar Waheed, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to gain an understanding of the depression-executive function syndrome hypothesis and identify potential avenues of treatment.

Summary:

Background

Late-onset depression has been conceptualized as neurological disease. Findings implicating dysfunction of frontostriatal-limbic

pathways in geriatric depression have led to the depression-executive dysfunction (DED) syndrome hypothesis.

Objective

To examine efficacy of atomoxetine in decreasing fatigue and executive dysfunction in patients with MDD.

Methodology

This prospective randomized open label experimental study included 20 patients (M=13, F=7, average age=41.3 years) with MDD. They were stabilized on antidepressants/mood stabilizers but still experienced fatigue and executive dysfunction. They had failed or were intolerant of bupropion and methylphenidate augmentation. Atomoxetine, 10 mg, was added to their treatment regimen increasing to 25 mg po qd after one week. Executive function and fatigue was assessed at baseline, one week, three weeks, six weeks and 12 weeks using the HAM-D, Trail A, Trail B and WAIS-III working memory subscales. Fatigue was measured on a subjective scale of 1-10.

Results

There was significant improvement in 14 patients, moderate improvement in 3 patients and no improvement in 3 patients.

Conclusions

Emerging research suggests depressive symptoms associated with executive dysfunction may be a target for novel pharmacological agents. Formal cognitive testing may be a useful adjunct in clinical evaluation of patients with MDD, at index episode and more particularly upon recovery.

References:

1. 1. Alexopoulos GS, Role of executive function in late-life depression, J Clin Psychiatry. 2003;64 Suppl 14:18-23.
2. 2. Austin MP, Mitchell P, Goodwin GM, Cognitive deficits in depression: possible implications for functional neuropathology, Br J Psychiatry. 2001 Mar;178:200-6.

NR230 Monday, May 22, 3:00 PM - 5:00 PM

Assessment of the Impact of Noradrenergic, Dopaminergic, and Cholinergic Medications on Fatigue and Executive Dysfunction Associated With MDD: A Two-Year Follow-Up

M.Z. Hussain, M.D. *Prince Albert Mental Health Center, Psychiatry, 2727 2nd Avenue West, Prince Albert, AB, t2n1t1, Canada*, Seema Hussain, M.D., Waqar Waheed, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to gain an awareness of the depressive-executive dysfunction syndrome hypothesis and be able to identify several medication options for its treatment

Summary:

Objective

To demonstrate relative efficacy of noradrenergic and cholinergic medications in decreasing fatigue and executive dysfunction in patients with MDD.

Significance

Studies in normal controls and depressed subjects are strongly suggestive of a close integration between the DLPFC, subgenual, cingulate, and frontostriatal limbic network in depression and executive dysfunction. Pharmacological alterations in the level of neurotransmitters associated with these brain regions may result in an improvement in the cognitive dysfunction and low energy associated with depressive illness.

Late-onset depression has been conceptualized as a neurological disease. Findings implicating dysfunction of frontostriatal-limbic pathways in geriatric depression led to the depression-executive dysfunction (DED) syndrome hypothesis.

Methodology

This prospective randomized open label experimental study included 60 patients with MDD (m =23, f =37, mean age = 45.8 years), stabilized on antidepressants/mood stabilizers but still experiencing fatigue and executive dysfunction. They were randomized to four groups to whom bupropion, modafinil, galantamine and supportive therapy were added to their therapeutic treatments respectively. Executive function and fatigue were assessed at baseline, 1, 3, 6 and 12 weeks and then at 3, 6,12, 18 and 24 months using the HAM-D, Trail Making A, Trail Making B and WAIS-III working memory subscales. Fatigue was measured on a subjective scale of 1-10.

Results

Clinically significant improvement in fatigue and executive dysfunction in the medication groups was tenfold greater as compared to the supportive therapy group and was maximal at 12 weeks.

Conclusions

Emerging research suggests DED syndrome may be a target for novel pharmacological agents. Formal cognitive testing may be a useful adjunct in clinical evaluation of patients with MDD, at index episode and more particularly upon recovery.

References:

1. Alexopoulos GS, Role of executive function in late-life depression, J Clin Psychiatry. 2003;64 Suppl 14:18-23.
2. Austin MP, Mitchell P, Goodwin GM, Cognitive deficits in depression: possible implications for functional neuropathology, Br J Psychiatry. 2001 Mar;178:200-6.

NR231 Monday, May 22, 3:00 PM - 5:00 PM

Frontal EEG at One Week Predicts Clinical Response to SSRI Treatment in MDD

Dan V. Iosifescu, M.D. *Massachusetts General Hospital, 50 Staniford Street, Suite #401, Boston, MA, 02114*, Scott D. Greenwald, Ph.D., Charles P. Smith, B.S., Philip H. Devlin, M.S., Jonathan E. Alpert, M.D., Sarah K. Hamill, B.A., Maurizio Fava, M.D.

Educational Objectives:

To understand the role of automated EEG analysis as a clinically useful predictor of treatment efficacy in major depressive disorder.

Summary:

Objective: To investigate the role of frontal EEG as predictor of clinical response to SSRIs in MDD.

Method: 84 subjects (mean age 36.1 + 12.9; 46.4 % female) meeting DSM-IV criteria for MDD entered an 8-week prospective treatment with open-label, flexible dose SSRIs. At each study visit (baseline, week 1, 4, and 8) we assessed MDD severity with the 17-item Hamilton Depression Rating Scale (HAM-D) and we recorded serial, 4-channel EEGs (F7-Fpz, F8-Fpz, A1-Fpz, A2-Fpz). An EEG index (Bis-Dep (rev 0.2)) was developed to predict clinical response using EEGs assessed at baseline and week 1. Clinical response was defined as HAM-D reduction at week 8 > 50%.

Results: 46 subjects (55%) responded to treatment. EEG predicted response with 73% accuracy overall (n=84). As expected, response prediction was better in the 22 subjects who received no SSRI dosage changes after week 1 compared to the 62 subjects who received dosage change after the second EEG assessment at week 1 (i.e., 86% versus 68%, $p < 0.05$).

Discussion: EEG response to initial dosing is predictive of clinical response. It is possible that the predictive accuracy in subjects receiving dosage adjustments would be enhanced by assessing EEG responses occurring 1 week following each dose change. We are testing this hypothesis currently in a prospective evaluation of this index in a large, multi-center trial.

Conclusion: It may be possible to develop an easy-to-use tool using automated analysis of frontal EEG to predict treatment efficacy after one week of antidepressant treatment. The EEG index predictive ability was best in subjects with no antidepressant dose change after week 1.

References:

1. Cook IA, et al: Early Changes in Prefrontal Activity Characterize Clinical Responders to Antidepressants. Neuropsychopharmacology 2002; 27:130-131.
2. Losifescu D, et al: Frontal EEG Predicts at One Week Predicts Clinical Response to SSRIs in MDD. 2005 APA Annual Meeting (#870).

NR232 Monday, May 22, 3:00 PM - 5:00 PM

Risperidone Monotherapy Versus Risperidone or Haloperidol Plus Sertraline for Major Depression With Psychosis: Results of a Pilot, Double-Blind, Placebo-Controlled Trial

Philip G. Janicak, M.D. *Rush University Medical Center, Psychiatry, 1720 West Polk (MFIV), Chicago, IL, 60612*, Sheila Dowd, Ph.D., Elizabeth A. Winans, Pharm.D., Mary Jane Strong, M.S.

Educational Objectives:

At the conclusion of this presentation, the participant should understand the complexity of treating depression with psychotic features; recognize the mood regulating effects of second generation antipsychotics; and discuss their potential benefits for treating this population.

Summary:

Rationale: Major depression with psychosis usually requires a combination of antidepressant plus antipsychotic to adequately treat. Recent evidence indicates that second generation antipsychotics (SGAs) such as risperidone (RISP) have mood regulating effects distinct from their antipsychotic effects. We conducted a pilot trial to clarify whether RISP monotherapy would be comparable to RISP plus sertraline (SERT) or haloperidol (HPDL) plus SERT.

Methods: After 3- to 7-day medication washout, 23 depressed subjects (19 unipolar; 4 bipolar) with psychotic features signed consent and 15 were randomized to RISP plus placebo (n=4); RISP plus SERT (n=5); or HPDL plus SERT (n=6) for 6 weeks. Medication doses ranged from 0.5 to 6 mg/day for RISP (week 2 mean=2.3 mg); 1 to 10 mg/day for HPDL (week 2 mean=4.4 mg); and 50 to 200 mg/day for SERT (week 2 mean=50 mg). Primary outcome measures were the Positive and Negative Syndrome Scale (PANSS), the Hamilton Depression Rating Scale (HDRS), and the Clinician-Administered Rating Scale for Mania (CARS-M).

Results: There were no significant differences among the three groups for relevant demographic variables or baseline ratings. Further, all three groups demonstrated a comparable percent improvement on the PANSS and HDRS total covariant adjusted baseline scores (LOCF). Based on the CARS-M, no patients demonstrated manic symptoms. Perhaps because of the relatively low doses of antipsychotics, Simpson-Angus Scale scores did not differ among the three groups at the end of the study.

Conclusion: Our pilot trial found comparable improvement in both psychotic and depressive symptoms in subjects receiving RISP alone, RISP plus SERT, or HPDL plus SERT. These results are consistent with less rigorously designed trials but will require replication with a larger sample.

References:

1. Baslet G, Nour H, Janicak PG: The role of second-generation antipsychotics in the treatment of mood disorders. Part II: depression. Contemporary Psychiatry 2003; 2(8):1-8.
2. Chan C, Janicak PG, Davis JM, Altman EA, Andriukaitis S, Hedeker D: Response of psychotic and nonpsychotic depressed patients to tricyclic antidepressants. J Clin Psychiatry 1987; 48:197-200.

NR233 Monday, May 22, 3:00 PM - 5:00 PM

Cognitive Function in Patients Receiving Open-Label Lamotrigine With or Without Concomitant Valproate, Antidepressants, or Antipsychotics

Neil Kaye *Thomas Jefferson University College of Medicine, 5301 Limestone Road #103, Wilmington, DE, 19808*, Jay Graham, Jeremy Roberts, Robert Leadbetter, Kevin Nanry

Educational Objectives:

At the conclusion of this presentation, the participant should be able understand patient response and tolerability to lamotrigine treatment.

Summary:

Objective: Lamotrigine improves self-rated cognitive function in patients with bipolar I disorder, with similar improvement seen in patients receiving lamotrigine monotherapy or polytherapy.[1] The current analysis examined the cognitive effects of lamotrigine in the setting of commonly co-administered medications in patients with bipolar I disorder.

Methods: A "post hoc" analysis evaluated changes in self-rated cognitive function in patients who were and were not receiving concomitant valproate, antidepressants, or antipsychotics. Data is from a prospective open-label study of lamotrigine[2] in 1175 patients with bipolar I disorder which was designed to assess the rate of rash in patients with and without specific dermatological precautions. Lamotrigine was administered for 12 weeks, including a 5-week titration period (target dosage 200 mg/day). Self-rated cognitive function was assessed with the Medical Outcomes Study Cognitive Scale (MOS-Cog) at baseline and week 12.

Results: Statistically significant improvement from baseline in MOS-Cog mean scores was observed in patients taking lamotrigine with (mean $\pm$ SD, 7.3 $\pm$ 23.92) and without (8.7 $\pm$ 22.17) concomitant valproate and in patients with (8.6 $\pm$ 22.43) and without (8.1 $\pm$ 22.83) antidepressants. While statistically significant improvement in mean scores of cognitive function was seen in patients with (5.7 $\pm$ 23.17) and without (9.6 $\pm$ 22.18) antipsychotics, patients taking lamotrigine without antipsychotics exhibited a statistically significantly greater degree of improvement ($P < 0.05$).

Conclusion: Lamotrigine improved self-rated cognitive function mean scores in patients taking lamotrigine with and without concomitant valproate, antidepressants, or antipsychotics; however, greater improvement was seen in patients without concomitant antipsychotics.

This study was supported by GlaxoSmithKline.

References:

1. Khan A, Ginsberg LD, Asnis GM, et al. Effect of lamotrigine on cognitive complaints in patients with bipolar I disorder. J Clin Psychiatry. 2004;65:1483-1490.
2. Ketter TA et al. The Effect of Dermatologic Precautions on the Incidence of Rash with Addition of Lamotrigine in the Treatment of Bipolar I Disorder. J Clin Psych. In Press.

NR234 Monday, May 22, 3:00 PM - 5:00 PM

A Retrospective Controlled Study Into Memory Complaints Reported by Depressed Patients Following Treatment With Electroconvulsive Therapy or Antidepressants

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Educational Objectives:

At the conclusion of this presentation, the participants should be able to recognize that patients who have been treated with electroconvulsive therapy (ECT) were more convinced that they suffered from retrograde amnesia due to their illness or treatment. This conviction is supported by objective test results.

Summary:

Objective: This study compared the levels of subjective and objective retrograde amnesia in depressed patients who received ECT or treatment with antidepressive medication.

Method: Patients who suffer from depression according to DSM IV criteria and were admitted within the past five years prior to this study in a general psychiatric hospital were screened for inclusion. Subjective retrograde amnesia was assessed using the Squire Subjective Memory Questionnaire (SSMQ) and the ECT Retrograde Amnesia and Perception Scale (ERAPS), a newly developed scale. Participants' Extended Release APS memory scores were compared with proxies' Extended Release APS memory scores of the patients in order to assess the reliability of memory complaints. Objective retrograde amnesia was assessed using the Autobiographical Memory Interview (AMI) and the Amsterdam Media Questionnaire (AMV).

Results: 20 of the 84 patients who received ECT and 30 of the 196 patients who received antidepressive medication participated in the study. A significant group difference was found for the patient's Extended Release APS memory score and the Amsterdam media questionnaire 1990's score. This difference could not be explained by the influence of determinants for retrograde amnesia. ECT patients equally attributed complaints about memory problems to the depression, treatment with medication and to ECT treatment.

Conclusions: These results showed that patients who have been treated with ECT (and their proxy) were more convinced that they suffered from retrograde amnesia due to their illness or treatment. This conviction was supported by objective test results. Future research should address the influence of this conviction on the willingness to receive ECT.

References:

1. Coleman EA, Sackeim HA, Prudic J, Devanand DP, McElhiney MC, Moody BJ: Subjective memory complaints prior to and following electroconvulsive therapy. Biol Psychiatry 1996;39:346-356.
2. Donahue AB: Electroconvulsive therapy and memory loss: a personal journey. J ECT 2000;16:133-143.

NR235 Monday, May 22, 3:00 PM - 5:00 PM

The Direct Medical Cost for Two Years and Physical Symptoms in Chronic Illness Patients With Depression

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Educational Objectives:

Depression in patients with chronic illness has been unrecognized and under treated. Futhermore chronic illness patients with depression have more physical symptoms and used more medical cares than patients without depression. Also direct medical costs of patients with depression are higher than those of patients without depression. We reconfirm that early diagnosis and treatment of depression with chronic illness is very important for the good outcome of illness, the quality of life of patients, and economy of chronic illness patients with depression.

Summary:

Objective: We screened the depression in chronic illness patients and compared the differences of the physical symptom severity and economic burden in patients with or without depression.

Method: The subjects were the medical patients(N=1155) of St. Mary's Hospital in Seoul who have been treated due to endocrine, cardiovascular, pulmonary, gastrointestinal, renal, or immunological diseases over 1 year in 2003 and 2004. The patients checked Zung Self-rating Depression scale and Patients Health Questionnaire(PHQ)-15. We compared the difference of direct medical costs, number of medical care of patients with or without depression in 2003 and 2004.

Results: The numbers of patients without depression, with mild, moderate, and severe by Zung's scale were 662, 254, 149, and 90. The means of direct medical costs of patients without depression, with mild, moderate, and severe depression were 1896, 2292, 2411, and 3005$ in 2003. The means of direct medical costs of patients without depression, with mild, moderate, and severe depression were 2479, 2973, 3518, and 3777$ in 2004. The numbers of patients with under 5 of PHQ score, with 6-10 of PHQ score, 11-15 of PHQ score, and over 16 of PHQ score were 579, 398, 135, and 43. The number of patients without depression, with mild, moderate, and severe depression in patients(N=43) with high PHQ score(>16) were 4, 5, 12, and 22. The patients with severe symptoms was higher in patients with severe depression.

Conclusion: In this study, 42.7% of patients with chronic illness had depression. The economic burden in 2003 and 2004, and the severity of symptoms of chronic illness patients with depression was higher than those of patients without depression. This study suggested that early diagnosis and treatment of depression in chronic illness patients is very important for the good outcome of illness, the quality of life, and economy of patients.

References:

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NR236 Monday, May 22, 3:00 PM - 5:00 PM

The Tryptophan Hydroxylase Polymorphism in Korean Patients With Bipolar Disorder

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize some biological basis for typology and genetic mechanism of bipolar disorder in Korea.

Summary:

Objective: This study has been carried out to explore the genetic causes of bipolar disorder by comparing the frequency of Tryptophan Hydroxylase(TPH) A218C polymorphism between bipolar disorder patients and normal controls, and to explore the relation between clinical characteristics of bipolar disorder patients and TPH polymorphism.

Methods: The genotype and allele frequencies of TPH in the genome of 113 hospitalized patients with bipolar disorder was compared with those of 124 normal control subjects using poly-

merase chain reaction and restriction fragment length polymorphism. The association between TPH A218C polymorphism and clinical characteristics in bipolar disorder patients were explored.

Results: The distributions of TPH A218C polymorphism between the patients with bipolar disorder and normal control subjects show no difference statistically. There was a significant difference in the distribution of TPH genotype by clinical characteristics. The frequency of C allele is significantly higher in patients with a history of suicidal attempts. The frequency of A allele is significantly higher in patients with family history of bipolar disorder.

Conclusion: This study suggests that suicidal attempts and family history in the patients with bipolar disorder are clearly associated with TPH A218C polymorphism and may explain, in part, the biological basis for these typologies.

References:

1. Mann JJ, Malone KM, Nielsen DA, Goldman D, Erdos J, Gelerter J: Possible association of a polymorphism of the tryptophan hydroxylase gene with suicidal behavior in depressed patients. Am J Psychiatry 1997;154:1451-1453.
2. Souery D, Van Gestel S, Massat I, Blairy S, Adolfsson R, Blackwood D, et al: Tryptophan hydroxylase polymorphism and suicidality in unipolar and bipolar affective disorders: a multcenter association study. Biol Psychiatry 2001;49:405-409.

NR237 Monday, May 22, 3:00 PM - 5:00 PM

Parallel Symptoms in Depressed Children and Depressed Mothers in a Clinic-Based Hungarian Sample

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Educational Objectives:

Educational Objectives: At the conclusion of this presentation, participants will be able to recognize the importance of maternal depression in the child's depression and some of the effects that might influence symptom presentation in the child. One such influence might be maternal reinforcement of certain depressive symptoms of the child and/or social modeling of other depressive symptoms of the mother by the child. These effects should also be considered in therapy.

Summary:

Objective: Mothers of depressed children often suffer from depression themselves. We investigated maternal and child affective symptoms to look for associations and/or similarities.

Method: Data were examined for 129 children (51 girls) from a clinic-based, multi-site study of childhood depression in Hungary. Children's symptoms and diagnoses were ascertained by a standardized semi-structured interview (ISCA-D) and independent diagnosticians; mothers completed the Beck Depression Inventory (BDI).

Results: Children's mean age of onset of depression was 11.92 years (sd: 2.3 years). More than 52% of mothers had BDI scores at/above the clinical cut-off (mean: 12.95, sd: 9.76). In comparing maternal and child depressive symptoms reported by mothers, sadness, indecision, and tiredness were found to be closely related. Parental reinforcement might play a role in these symptoms. When the child was the informant, tiredness and guilt correlated only in girls and mothers, suggesting that these symptoms may partly represent social modeling.

Conclusion: Given symptom similarities between mothers and children, therapy should consider mechanisms of symptom reinforcement or modeling.

At the conclusion of this presentation, participants will be able to recognize the importance of maternal reinforcement of certain depressive symptoms in the child and the possibility of modeling of other depressive symptoms.

References:

1. Goodman SH, Gotlib IH: Risk for Psychopathology in the Children of Depressed Mothers: A Developmental Model for Understanding Mechanisms of Transmission. Psychol Review 1999; 106:458-490.
2. Sherrill JT, Kovacs M: Interview Schedule for Children and Adolescents (ISCA). J Am Acad Child Adolesc Psychiatry 2000; 39:67-75.

NR238 Monday, May 22, 3:00 PM - 5:00 PM

Development and Reliability of a Combined Hamilton Depression, Anxiety, and Atypical Symptoms Scale

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the psychometric and interrater reliability data on a new scale designed to combine the Hamilton Depression (SIGHD) and Anxiety (SIGHA) Scales, and the Atypical Depression Scale (SIGH-ADS).

Summary:

Background: In clinical depression trials, investigators are often interested in measuring multiple symptom domains. The widely-used Hamilton Depression and Anxiety Scales have considerable overlap, with probes often being unnecessarily repeated when the scales are administered sequentially. A combined HAMD and HAMA interview was developed, the SIGH-AD (Williams, 1996), which eliminates redundancy yet allows both scales to be rated simultaneously. Another problem is the HAMD fails to assess atypical symptoms of depression. In order to provide a comprehensive scale that measures all these symptom domains, we developed a comprehensive scale that combines the HAMD, HAMA, and the atypical HAMD items developed by Williams & Terman (SIGH-ADS; 2003). An interview guide was also developed that includes additional probes and anchor clarifications to improve reliability.

Method: 14 raters conducted a total of 35 paired interviews using one of two methodologies: direct observation (n=25) or independent interviews (n=10). In both cases raters scored the interviews blind to the others' ratings. After ratings were logged, raters discussed scoring discrepancies. All raters went through a web tutorial on scoring conventions prior to reliability testing, and had one group practice session. Newer raters were paired with experienced raters to enhance learning, and observed sessions occurred prior to independent sessions.

Results: The inter-rater reliability (ICC) for total scale score was .95(p=.0001). Subscale ICC's were .93, .91, and .95 for the 17-item HAMD, HAMA, and atypical HAMD items respectively ($p < .0001$ for all comparisons). When just the independent interviews were examined, the ICC's were .97(total-scale), .94(17-item), .86 (HAMA), and .87(atypical symptoms).**Conclusions:** A comprehensive structured interview for assessing a wide range of symptoms of depression and anxiety demonstrates good to excellent inter-rater reliability, when used in conjunction with prior didactic training. Such a tool can be useful and time-efficient in studies requiring the comprehensive assessment of symptomatology.

References:

1. Williams JBW: A structured interview guide for the Hamilton Depression Rating Scale. Arch Gen Psychiatry. 1988 Aug;45(8):742-7.

2. Williams JBW, Terman M: Structured Interview Guide for the Hamilton Depression Rating Scale with Atypical Depression Supplement (SIGH-ADS), 2003 rev., New York, New York State Psychiatric Institute.

NR239 Monday, May 22, 3:00 PM - 5:00 PM

A Retrospective Analysis of the Effects of Bupropion XL (Wellbutrin XL®) Versus Sertraline (Zoloft®) and S-Citalopram (Lexapo®) on Pleasure, Concentration, Interest and Energy in Patients With MDD

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to identify differential effects of bupropion XL, s-citalopram, and sertraline on specific core symptoms of depression: pleasure, interest, energy and concentration. Participants will also be introduced to a novel patient assessment and monitoring tool used to evaluate patients with major depressive disorder. This tool was used at baseline and post initiation of therapy to evaluate the changes in these core symptoms.

Summary:

Objectives

The objective of this study is to evaluate the effectiveness of extended-release bupropion hydrochloride compared to sertraline, and s-citalopram on pleasure, concentration, interest, and energy in patient's with MDD.

Study Design / Methods

The study included a retrospective chart review of patients with MDD evaluating changes in responses to the PROS-D patient assessment and monitoring questionaire. PROS-D is a 10 item (based on DSM-IV) questionaire. Each item is rated by the patient from 0-4 (absent to extreme). Changes in responses to the following items will be analyzed:

Item 1: Sad or Depressed Mood (Pleasure)
Item 2: Interest in Activities / People, (Interest)
Item 4: Tiredness and Fatigue (Energy) and
Item 5: Difficulty Concentrating (Concentration)

Results

The mean change from baseline for bupropion was -1.21, -0.93, -1.43, and -1.29 for Items #1, 2, 4, and 5 respectively. The mean change from baseline for sertraline was -1.44, -1.11, -0.56, and -0.56 for Items #1, 2, 4, and 5 respectively. The mean change from baseline for escitalopram was -0.85, -0.92, -0.46, and -0.46 for Items #1, 2, 4, and 5 respectively. There was significant improvement in each group.

Conclusion:

Many patients with major depression present with low energy, diminished pleasure, and an inability to concentrate. As these symptoms typically respond well to antidepressants with noradrenergic and/or dopaminergic effects, bupropion would appear to be an effective treatment choice for patients with these symptoms. Based on these data, the average change in energy and concentration favored bupropion when compared to both escitalopram and sertraline. The average change in pleasure and interest was also greater with bupropion when compared to escitalopram; although numerically lower than sertraline. As limited by a relatively small sample size and retrospective nature, larger controlled analysis are needed to duplicate and confirm these findings.

References:

1. Preskorn SH: Bupropion: What Mechanism of Action? Journal of Psychiatric Practice 2000; 6: 39-44.
2. Stahl SM et al: A review of the neuropharmacology of bupropion, a NE and DA reuptake inhibitor. J Cln Psych 2004; 6: 159-66.

NR240 Monday, May 22, 3:00 PM - 5:00 PM

Feeling Blue? Using Colour Shift to Characterize Mood Cyclicity in Health and Bipolar Disorder

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Educational Objectives:

appreciate how time-series analysis of mood can characterize mood phenomenology and constrain candidate models of mood.

Summary:

Purpose: Mood cyclicity is poorly characterised: whereas some models of mood disorders (e.g., SAD and PMDD) imply that mood variation is dominated by a single frequency, other work suggests that mood varies at multiple frequencies simultaneously over time, similar to white noise. To better characterise mood cycling in illness and health, we examined power spectra created using 18-month time series from subjects with bipolar disorder and healthy controls.

Method: Mood self-report ratings were collected every 12 hours over 18 months from (n=19) subjects with rapidly-cycling bipolar disorder and (n=19) healthy controls using a 19-item visual analog scale (VAS)-based questionnaire on handheld computers (HHC's) [Ref 1]. The use of HHC's ensured temporal accuracy, guarded against retrospective recall, and minimized data loss. One questionnaire item, asking subjects to rate their "current mood," using anchors "worst ever" and "best ever," was used to create a time series for each subject's global mood. We used Lomb's method to calculate the contribution of cycles ranging from 1/day to 1/500 days. Non-linear least-squares regression was used to fit spectra over middle frequencies.

Results: 10/38 subjects' spectra were "white," with broadband contribution; 28/38 were red-shifted -- broadband with low-frequency predominance; no blue shifts or prominent spectral peaks were observed. The mean slopes of both groups were significantly reddened; no significant difference between slopes in disease states, sexes, or ages was found.

Conclusions: Mood variation is typically broadband and red-shifted. Adequate models of mood will need to explain this finding: while kindling models cannot predict this result, self-organized critical (SOC) models can [Ref 2]. Further investigation is necessary to determine if differences can be detected between bipolar and control groups.

References:

1. Kreindler, D, Levitt, A, Woolridge, N, and Lumsden, CJ. Portable mood mapping: the validity and reliability of analog scale displays for mood assessment via hand-held computer. Psychia Res 2003; 120(2): 165-177.
2. Kreindler DM and Lumsden CJ: The Effects of Irregular Sampling and Missing Data in Time Series Analysis. Nonlinear Dynamics, Psychology, and Life Sciences 2006 (in press).

NR241 Monday, May 22, 3:00 PM - 5:00 PM

Long-Acting, Injectable Risperidone in Frequently Relapsing Bipolar Disorder

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Educational Objectives:

At the conclusion of this presentation, participants will be able to differentiate the characteristics of patients with frequently relapsing bipolar disorder (FRBD) and recognize the role of a long-acting, atypical antipsychotic in addressing unmet needs in this difficult-to-treat patient population.

Summary:

Objective: A subset of patients with bipolar disorder (BD) relapse frequently and experience particularly high levels of morbidity and poor outcomes. This trial evaluates the addition of long-acting risperidone (LAR) to treatment-as-usual on mood symptom control and functioning in patients with frequently relapsing BD (FRBD).

Methods: Patients meeting criteria for BD and experiencing ≥4 episodes requiring clinical intervention in the past 12 months and ≥2 episodes in the past 6 months, received open-label (OL) augmentation of treatment-as-usual with LAR (25-50 mg) for 16 weeks. Remitters (Young Mania Rating Scale [YMRS] and Montgomery-Asberg Depression Rating Scale [MADRS] ≤10 over the last 4 weeks of OL) were eligible for randomization to placebo or LAR in a double-blind (DB), 52-week, relapse-prevention phase. Measures included MADRS, YMRS, and Clinical Global Impressions of Severity (CGI-S). OL results for the first 84 patients are reported.

Results: At baseline, 64% of patients were moderately-markedly ill by CGI-S; 37% scored ≥20 on YMRS; 38% scored ≥20 on MADRS. Mean (±SD) YMRS and MADRS scores were 15.7±10.9 and 12.7±11.3, respectively. Seventy-four percent completed the OL phase; 49% met remission criteria and were eligible to enter DB phase; 25% did not meet remission criteria but continued OL LAR treatment. Reasons for discontinuation from OL phase included: adverse events (6%); lost to follow-up (1%); noncompliance (1%); protocol violation (1%); withdrawal of consent (17%). At OL endpoint, the percent of patients with CGI-S scores of moderately ill or worse decreased to 19% (from 64%) and mean (±SD) YMRS and MADRS improvements were -10.4±11.3 (P<0.001) and -4.5±12.6 (P<0.05), respectively.

Conclusions: Preliminary OL findings suggest addition of long-acting risperidone to treatment as usual may reduce symptoms for patients with frequently-relapsing bipolar disorder. Long-term, double-blind, placebo-controlled data from this ongoing trial will indicate the validity of these early observations.

Source of Funding: Janssen, LP.

References:

1. Schneck CD, Miklowitz DJ, Calabrese JR, Allen MH, Thomas MR, Wisniewski SR, Miyahara S, Shelton MD, Ketter TA, Goldberg JF, Bowden CL, Sachs GS: Phenomenology of rapid-cycling bipolar disorder: data from the first 500 participants in the Systematic T.

2. Vieta E, Calabrese JR, Hennen J, Colom F, Martinez-Aran A, Sanchez-Moreno J, Yatham LN, Tohen M, Baldessarini RJ: Comparison of rapid-cycling and non-rapid-cycling bipolar I manic patients during treatment with olanzapine: analysis of pooled data. J.

NR242 Monday, May 22, 3:00 PM - 5:00 PM

Theory of Mind and Psychotic Symptoms in Bipolar Disorder

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the relationship between the "theory of mind" deficit and the development of psychotic symptoms in bipolar disorder.

Summary:

Introduction: Recent data have shown a familial aggregation of psychotic symptoms in bipolar disorder pedigrees, suggesting the value of the psychotic bipolar subtype in psychometric, genetic and biological investigations. The Theory of Mind (ToM), or "the ability to attribute mental states to self and others in order to predict their behaviour", is impaired in schizophrenic patients, but there are few studies in bipolar patients. An impairment of the ToM could characterize the subgroup of bipolar patients who develop psychotic symptoms during their illness.

Objective: To asses the ToM in a sample of euthymic bipolar patients with and without a history of psychotic symptoms during their illness.

Method: 47 patients meeting DSM-IV criteria for Bipolar Disorder type I were recruited. They were described as euthymic by their consultants, but Hamilton Rating Scale (< 8)and Young Mania Rating Scale (<8) were used in order to confirm it. The sample was divided in two groups: 25 of the 47 patients had a positive history of psychotic symptoms, after been assessed with the the Schedule for Affective Disorders and Schizophrenia -Lifetime Version (SADS-L), and 22 had not. They all had had three or more affective relapses. Patients were assessed with the Spanish adapted version of the "Advanced ToM Test" (Happé, 1994), and Asarnov Test and Wisconsin Test in order to control the cognitive general function.

Results: Mean age of the sample population was 46.2 years, and 17,8 years was the mean duration of the illness. After controlling for age and length of illness, the two groups performance in the ToM task did not differ significantly. Attention and executive functions were also similar between the groups.

Conclusion: our data do not support the idea of a ToM impairment as a marker associated with the development of psychotic symptoms in a sample of euthymic bipolar patients.

References:

1. Potash JB, Willour VL, Chiu YF, Simpson SG, Mackinnon DF, Pearlson GD, DePaulo JR, McInnis MG. The familial aggregation of psychotic symptoms in bipolar disorder pedigrees. Am J Psychiatry 2001; 158: 1258 - 1264.

2. Herold R, Tenvy T, Lénard K, Trixler M. Theory of mind deficit in people with schizophrenia during remission. Psychological Medicine, 2002; 32: 32: 1125-1129.

NR243 Monday, May 22, 3:00 PM - 5:00 PM

Escitalopram and Citalopram in the Treatment of MDD: Effect of Baseline Severity

Raymond W. Lam, M.D. *University of British Columbia, Psychiatry, 2255 Wesbrook Mall, Vancouver, BC, V6T 2A1, Canada*, Henning F. Andersen

Educational Objectives:

At the conclusion of this presentation, the participant will be able to evaluate the efficacy of escitalopram compared to citalopram.

Summary:

Objective: Pooled analyses from pivotal trials have consistently indicated advantages of escitalopram versus citalopram, especially in patients with more severe depression (1,2). The objective of this study was to critically examine the effect of baseline severity on the efficacy of escitalopram versus citalopram.

Methods: All studies of patients with MDD that included comparisons of escitalopram, citalopram and placebo were selected and the results pooled for analysis. Treatment outcome was assessed by scores from the Montgomery-Åsberg Depression Rating Scale (MADRS) at 8 weeks of treatment. The interaction of baseline severity as assessed by MADRS score and the treatment effects of escitalopram and citalopram were tested in an ANCOVA model adjusting for baseline severity, centre and treatment.

Results: Two flexible dose and 1 fixed dose placebo-controlled studies involving patients with moderate to severe MDD were included in the pooled analysis. The fixed dose study examined escitalopram 10 mg and 20 mg versus citalopram 40 mg, so the 10 mg arm was excluded to ensure that similar doses of escitalopram and citalopram were compared (exclusion of this arm did not affect statistical significance of the analyses). Results of the pooled analysis showed that the differences between escitalopram and placebo (p=0.001 for no trend) and between escitalopram and citalopram (p=0.0012 for no trend) increased with increasing baseline severity of MDD; in contrast, the difference between citalopram and placebo was rather constant relative to baseline severity. In addition, there was a superior effect of escitalopram on response to treatment (defined as ≥50% decrease in MADRS total score) at week 8 compared to placebo regardless of baseline severity, and compared to citalopram at higher levels of baseline severity.

Conclusion: These results indicate that in the treatment of MDD, escitalopram is superior to citalopram in patients with more severe depression.

Acknowledgments: Studies funded by H. Lundbeck A/S.

References:

1. Gorman J, Korotzer A, Su G. Comparison of escitalopram and citalopram in the treatment of major depressive disorder: Pooled analysis of placebo-controlled trials. CNS Spectr 2002; 7(4 Suppl):40-44.

2. Lepola U, Wade A, Andersen HF. Do equivalent doses of escitalopram and citalopram have similar efficacy? A pooled analysis of two positive placebo-controlled studies in major depressive disorder. Int Clin Psychopharmacol 2004, 19:149'155.

NR244 Monday, May 22, 3:00 PM - 5:00 PM

Traumatic Brain Injury and MDD: The Role of the Serotonin Polymorphisms in Treatment Outcome

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Educational Objectives:

At the conclusion of this poster, the participant will be aware of the possible clinical utility of polymorphisms in predicting response to antidepressant treatment in patients with traumatic brain injury.

Summary:

Objective

Traumatic brain injury (TBI) is associated with damage to the serotonergic (5-HT) system, a high prevalence of MDD, and variability in response to antidepressant treatment. We examined whether polymorphisms of the 5HT transporter promoter region (5-HTTLPR; short [S] or long [L]) and 5-HT_{2A} receptor (T102C) genes predicted tolerability and treatment response to 5-HT pharmacotherapy in depressed TBI patients.

Methods

Mild-to-moderate TBI patients with MDD (DSM-IV criteria) received citalopram (20-40 mg/day, p.o.). Treatment response was assessed using the Hamilton Depression Rating Scale (response: ≥50% decrease HAMD17). Genotyping was done blind to treatment.

Results

Of 46 depressed TBI patients (mean age 39.2 ±18.9, 24M/22F), 36 (78%) completed 6 weeks of citalopram and 9 (25%) were responders. Backward regression analysis (ITT group, n=39) indicated past psychiatric history (p=.003) and L allele (n=15, p=.048) were associated with better treatment response (F=6.4, p=.005) and accounted for 32% of the variance. There was a trend for an increased proportion of drop outs with CC genotype (n=9)(44% versus 16%; Fisher's, p=.087).

Conclusions

These preliminary findings suggest that genotype may impact treatment outcome following citalopram in the depressed TBI population. It remains to be seen if this translates to important differences in long term outcomes.

References:

1. Journal Article - Rapoport M, McCullagh S, Streiner D, Feinstein A: The Clinical Significance of Major Depression Following Mild Traumatic Brain Injury. Psychosomatics 2003; 44: 31-37.

2. Journal Article - Chan F, Lanctôt KL, Rapoport M, Herrmann N, McCullagh S, Feinstein A. Traumatic brain injury and depression: assessing the role of the serotonin transporter promoter polymorphism. Can J Clin Pharm 2005; 12:e117.

NR245 Monday, May 22, 3:00 PM - 5:00 PM

The Comparison of Sociodemographic and Clinical Characteristics Between Patients With Early Onset and Late Onset Bipolar Disorder

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that poor response to the treatment and family psychiatric histories were identified in early onset bipolar group.

Summary:

Objective: Bipolar disorder is charaterized by various clinical outcomes. Recently, much focus on the clinical characterization of bipolar disorder in relation to onset age has been made. This study is designed to investigate the sociodemographic and clinical characters according to onset age.

Method: We investigated hospital records (from 1990 to 2005) of 16 early onset (onset age before 20 in years) and 29 late onset (onset age after 40 in years) patients with type I or type II bipolar disorders and compared the sociodemographic and clinical characters between two patient groups.

Results: The mean onset age of early onset group was 16.5±1.96 in years and that of late onset group 50.3±8.91 in years. More family psychiatric histories were identified in early onset group (50% versus 13.8%, p<0.009). Poorer clinical status on discharge were also observed in early onset group (75% versus 37.9%, p<0.05). No significant difference in the hospital stay was found. Although not statistically significant, family history of mood disorder (66.7% versus 33.3%, p<0.087) and alcohol dependence (t=1.99, p=0.053) were more frequently identified in early onset group. We found higher rate of first depressive episode in late

onset group (4.1% versus 6.3%, p<0.133). No significant differences in symptoms and treatment were observed.

Conclusions: Poor response to the treatment and family history were identified in early onset group. Given the limitation that same diagnostic criteria were applied to both groups were taken into consideration, the results of observed differences according to the onset age in this study could be used in the classification of bipolar disorder.

References:

1. Marion Leboyer, Chantal Henry, Marie-Laure Paillere-Martinot and Frank Bellivier: Age at onset in bipolar affective disorders: a review. Bipolar Disord 2005: 7: 111'118.
2. Sajatovic M, Bingham CR, Campbell EA, Fletcher DF: Bipolar disorder in older adult inpatients. J Nerv Ment Dis. 2005 Jun;193(6):417-9.

NR246 Monday, May 22, 3:00 PM - 5:00 PM

Manic Behaviour Induced by Deep Brain Stimulation in Parkinson's Disease: Evidence of Substantia Nigra Implication?

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to know that manic behaviour could be link to the stimulation of the STN.

Summary:

Aims: To report the case of a patient who had benefited from bilateral subthalamic nucleus deep brain stimulation (STN-DBS) for Parkinson's disease and who presented acute and reproducible manic behaviour according to the stimulation conditions.

Manic behaviour linked to the stimulation of the STN area has been described but the pathophysiology of this complication is unknown.

Methods: Mood swings were assessed in a double-blind fashion using the Bech and Rafaelsen manic scale (MAS) in five conditions: no stimulation, bilateral stimulation with mania, bilateral stimulation without mood changes and cross stimulation.

The contacts location was determined by automatized matching of the post operative MRI with the stereotactic preoperative coronal MRI and by a stereotactic matching of the X-Rays controls performed at the end of surgery and of the preoperative MRI.

A PET scan using $H_2{}^{15}O$ was performed in three conditions (no stimulation, stimulation without mood changes and with mania).

Results: The manic behaviour was specifically induced by a bilateral stimulation of the deepest contacts both located in the Substantia nigra (SN).

Compared to STN stimulation without mood disorders, mania was associated with an increase of rCBF in the right superior frontal gyrus, dorsolateral prefrontal cortex, inferior temporal gyrus and lateral premotor cortex as well as in the left anterior cingulate cortex. Simultaneously, a decrease of rCBF was noted in the left insula, inferior parietal lobe and superior temporal gyrus.

Conclusion: The modifications of cortical activation related to mania in our patient are subcortically driven, involving the SN.

References:

1. Bearden CE, Hoffman KM, Cannon TD. The neuropsychology and neuroanatomy of bipolar affective disorder: a critical review. Bipolar Disord 2001; 3: 106-150; discussion 151-153.
2. Bejjani BP, Damier P, Arnulf I, et al. Transient acute depression induced by high-frequency deep-brain stimulation. N Engl J Med 1999; 340: 1476-1480.

NR247 Monday, May 22, 3:00 PM - 5:00 PM

Ziprasidone Does Not Exacerbate Mania or Induce Depression in the Treatment of Bipolar Mania

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Educational Objectives:

Participants will gain an understanding of the rates of emergent mania and depression in ziprasidone bipolar mania clinical trials.

Summary:

Objective: To assess the rates of manic exacerbation and emergence of depression in ziprasidone treatment of patients with bipolar mania.

Methods: Data from 2 similarly designed randomized, placebo-controlled trials of ziprasidone treatment in bipolar mania[1,2] were pooled and examined for the exacerbation of mania and emergence of depression. Exacerbation of mania was defined as a baseline to endpoint worsening in MRS score of ≥20%. Treatment-emergent depression was defined as a baseline to endpoint worsening in HAM-D score of ≥20% and a HAM-D score of ≥15 at endpoint.

Results: The proportion of patients treated with ziprasidone experiencing exacerbation of mania was low (5.2%) and significantly less than those patients treated with placebo (10.7%, P = 0.05). The proportion of patients treated with ziprasidone who experienced a treatment-emergent depression was similarly low (1.9%) and not significantly different from patients treated with placebo (4.6% P = NS).

Conclusion: This post hoc analysis suggests that ziprasidone is not associated with manic exacerbation or the emergence of depression in bipolar patients with acute bipolar mania.

Support for this study was provided by Pfizer Inc

References:

1. Keck PE Jr, Versiani M, Potkin S, West SA, Giller E, Ice K, Ziprasidone in Mania Study Group. Ziprasidone in the treatment of acute bipolar mania: a three-week, placebo-controlled, double-blind, randomized trial. Am J Psychiatry 2003;160:741-748.
2. Potkin SG, Keck PE Jr, Segal S, Ice K, English P. Ziprasidone in acute bipolar mania: a 21-day randomized, double-blind, placebo-controlled replication trial. J Clin Psychopharmacol 2005;25:301-10.

NR248 Monday, May 22, 3:00 PM - 5:00 PM

Quetiapine Monotherapy Demonstrates Efficacy in Reducing Suicidality in Bipolar Depression

Wayne Macfadden, M.D. *Astrazeneca Pharmaceuticals LP, 1800 Concord Pike, PO Box 15437, Wilmington, DE, 19850-5437,* Margaret Minkwitz, Elinor Spong

Educational Objectives:

At the conclusion of this session, participants will be able to evaluate the efficacy of quetiapine in improving suicide-related symptoms in depressive episodes of bipolar disorder.

Summary:

Objective: To investigate the effect of quetiapine monotherapy on measures of suicidality in depressive episodes in patients with bipolar disorder.

Methods: Patients with bipolar I or II depression (DSM-IV) were randomized to 8 weeks of quetiapine (300 or 600 mg/d) or placebo in two studies (BOLDER I[1] and II). A post-hoc analysis of 1045 patients from these studies evaluated the effects of quetiapine, compared with placebo, on suicidality at Week 8. Suicidality was measured using MADRS item 10 ("Suicidal thoughts") and HAM-D item 3 ("Suicide") scores, which were evaluated using mixed-effect model, repeated-measures analysis. Suicidal ideation and behavior were also evaluated (by 3 blinded reviewers) during the study using the Columbia suicidality criteria.[2]

Results: There were no cases of completed suicide during the two studies. The mean MADRS item 10 score decreased significantly more with both quetiapine doses than with placebo at Week 8 (300 mg/d: -0.98; $P<0.001$; 600 mg/d: -0.92; $P=0.001$; versus placebo: -0.64). The decrease in HAM-D item 3 score at Week 8 was also significantly greater with both quetiapine doses than with placebo (-0.62 and -0.57 versus -0.50; both $P<0.001$). The incidences of suicidal ideation (300 mg/d: 1.1%, 600 mg/d: 0.9%, placebo: 1.4%) and possible suicide attempts (0.3%, 0.9%, 0.3%) identified using the Columbia criteria were found to be low and similar in all three treatment groups during the two studies.

Conclusion: These findings suggest that quetiapine monotherapy, compared to placebo, does not increase, and may decrease, suicidal tendencies during depressive episodes of bipolar I or II disorder.

Supported by funding from AstraZeneca Pharmaceuticals LP.

References:

1. Calabrese JR, Keck PE, Jr., Macfadden W, Minkwitz M, Ketter TA, Weisler RH, et al. A randomized, double-blind, placebo-controlled trial of quetiapine in the treatment of bipolar I or II depression. Am J Psychiatry 2005;162(7):1351-60.
2. Background information on the suicidality classification project: What is the suicidality classification project and why is it necessary? 2004 [cited 2005 Nov 28]. Available from http://www.fda.gov/cder/drug/antidepressants/classificationProject.htm.

NR249 Monday, May 22, 3:00 PM - 5:00 PM

Hepatitis C Testing, Infection, and Treatment Rates Among Patients With Bipolar Disorder and Substance Use Disorders

Annette M. Matthews, M.D. *Portland VA Medical Center, Psychiatry, 3591 S.E. Francis, #E, Portland, OR, 97202,* Peter Hauser, M.D.

Educational Objectives:

Educational Objectives: Participants should know that hepatitis C has been targeted as the most important emerging blood-born pathogen in the Veteran's Health Administration (VA) system, and that this has resulted in many interventions to improve care for those with HCV. In this presentation, participants will learn the incidence of HCV in VISN 20 and the rates of screening, testing, and treatment for the disorder. In many healthcare systems, bipolar disorder and/or substance abuse disorder are associated with decreased access to treatment for hepatitis C. Participants will learn that in VA VISN 20 the rates of treatment for those with bipolar disorder with HCV are statistically the same as controls and possible conclusions from this finding will be explored.

Summary:

Objective/Hypothesis: To determine the hepatitis C (HCV) prevalence, screening, testing, and treatment rates of those with bipolar disorder and/or substance dependence as compared to those without either disorder in VISN 20 of the Veterans Affairs Healthcare System. Our hypothesis is that screening and testing rates will be greater for those with bipolar disorder and/or substance dependence when compared to controls, but that treatment rates will be the same or less that those in the control group.

Method/Proposed Methods: Using a medical record database, information was retrospectively collected on 325,410 patients within VISN 20 of the Northwest Veterans Healthcare Administration. We then compared HCV prevalence, screening, testing, and treatment rates among four groups: those with 1) bipolar disorder and no substance abuse; 2) those with substance use disorder, and no bipolar disorder; 3) those with co-occurring bipolar disorder and substance use disorder; and 4) those without either bipolar disorder or substance abuse. Incidence rates and relative risks were determined and compared across groups.

Discussion/Significance: Patients with bipolar disorder, substance use disorders, and co-occurring disorders are at increased risk for HCV infection as compared with controls. Relative to controls, individuals with substance use disorders and no bipolar disorder are statistically less likely to receive treatment for HCV than controls. However, bipolar patients, and patients with co-morbid bipolar disorder and substance abuse are statistically as likely to receive HCV treatment as controls. This suggesting that recent efforts to expand treatment to high risk populations within the Veterans Healthcare Administration may be having an impact on clinical practice.

References:

1. National Institutes of Health: National Institutes of Health Consensus Development Conference Statement: Management of hepatitis C: 2002 - June 10-12, 2002. Hepatology 2002; S3-S20.
2. Mishra G. Sninsky C. Roswell R. Fitzwilliam S. Hyams KC: Risk factors for hepatitis C virus infection among patients receiving health care in a Department of Veterans Affairs hospital. Digestive Diseases & Sciences 2003; 48: 815-20.

NR250 Monday, May 22, 3:00 PM - 5:00 PM

Quetiapine augmentation for treatment-resistant depression

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Educational Objectives:

Educational objective: At the conclusion of this presentation, the participants should be able to describe the benefits of augmenting SSRI/SNRI treatment with quetiapine in patients with treatment-resistant depression.

Summary:

Objective: Growing evidence supports augmentation of antidepressant therapy with atypical antipsychotics in treatment-resistant depression (1,2). This study investigated augmenting concurrent treatment with quetiapine in depressed patients partially responsive to SSRI/SNRI treatment.

Methods: In this 8-week, double-blind, placebo-controlled trial, patients (18-65 years) with baseline HAM-D17 scores ≥20 following 8 weeks SSRI/SNRI treatment were randomized to receive quetiapine (200-400 mg) or placebo as augmentation to SSRI/SNRI treatment. Efficacy measures included HAM-D17, MADRS, CGI-S, and CGI-I at study end.

Results: Baseline HAM-D17 scores were 25.0 and 24.5, and baseline MADRS scores were 32.5 and 33.5, for quetiapine (mean dose 268 mg/day, n=23) and placebo (n=13), respectively. Following treatment, patients receiving quetiapine had significantly lower HAM-D17 scores versus placebo (8.3 versus 14.7, respectively, $p<0.01$). More patients receiving quetiapine responded to treatment (≥50% reduction in HAM-D17 score) (67% versus 27%, p=

0.015), and achieved remission (HAM-D17 score <7) (43% versus 15%, p<0.05), versus placebo. Patients receiving quetiapine had significantly lower MADRS (15.4 versus 24.8, p<0.02), CGI-S (3.0 versus 4.0, p<0.03) and CGI-I (2.6 versus 3.5, p<0.04) scores versus placebo. Quetiapine treatment was generally well-tolerated.

Conclusion: Quetiapine augmentation of SSRI/SNRI treatment may benefit patients with treatment-resistant depression and warrants further investigation.

References

1. Barbee JG, Conrad EJ, Jamhour NJ: The effectiveness of olanzapine, risperidone, quetiapine, and ziprasidone as augmentation agents in treatment-resistant MDD. J Clin Psychiatry 2004; 65:975-981

2. Kennedy SH, Lam RW: Enhancing outcomes in the management of treatment resistant depression: a focus on atypical antipsychotics. Bipolar Disord 2003; 5 Suppl 2:36-47

References:

1. Barbee JG, Conrad EJ, Jamhour NJ: The effectiveness of olanzapine, risperidone, quetiapine, and ziprasidone as augmentation agents in treatment-resistant major depressive disorder. J Clin Psychiatry 2004; 65:975-981.

2. Kennedy SH, Lam RW: Enhancing outcomes in the management of treatment resistant depression: a focus on atypical antipsychotics. Bipolar Disord 2003; 5 Suppl 2:36-47.

NR251 Monday, May 22, 3:00 PM - 5:00 PM

Depression Effects on Outcomes in Cardiac Rehabilitation Programs

Ronald A. McGinnis, M.D. *Medical University of Ohio, Psychiatry, 3747 Sulphur Springs Rd, Toledo, OH, 43606-2627*, Angele McGrady, Ph.D., Dalynn Badenhop, Ph.D., Muhammad Rajput, M.D., Bradly W. Chapman, M.S., Michelle K. Bentle, B.A.

Educational Objectives:

Objectives:

1. Recognize the interaction between mood and anxiety symptoms and a patient's ability to participate in a cardiac rehabilitation program.

2. Describe the outcomes of patients who complete a cardiac rehabilitation program in regards to mood, anxiety and exercise ability.

Summary:

Purpose:

Anxiety and depressive disorders are common in patients who participate in cardiac rehabilitation programs and may complicate outcomes. The purpose of this study is to describe the influence of depression and anxiety on a population of patients undergoing cardiac rehabilitation.

Methods:

266 patients met entry criteria for participation in the cardiac rehabilitation program. At the interview session, patients gave informed consent and completed the Beck Depression Inventory II (BDI-II), Beck Anxiety Inventory (BAI) and SF-36 mental and physical health sections. One week later, 219 patients returned for the twelve minute walk test (WT) and began the program. Assessments were repeated at the end of the program.

Results:

Approximately half of the patients who signed the consent form did not complete the program (n=133). Those who completed the program were compared to non-completers on the dependent variables. Completers' BDI-II averaged 8.8 (7.8) while non-completers averaged 11.4 (8.6) ($p < 0.01$). Scores on the SF physical health measure were higher in the completers (38.5 (0.84)) than the non-completers (35.1 (.9)); $p < .005$. However, completers score on the SF mental health measure were significantly lower ($p < .05$) than those of non-completers (44.5 and 47.7 respectively). There were no differences in the number of feet walked (WT) or in the BAI between completers and non-completers.

Comparison of outcome data showed significant ($p < .05$) increases in WT and decreases in BDI-II, and BAI in those who completed the program.

Conclusions:

The results of this study suggest that anxiety and depressive symptoms improve significantly in those who complete a cardiac rehabilitation program. Depressive symptoms however are related to non-completion of cardiac rehabilitation. Assessment and treatment of depression are needed in cardiac rehabilitation patients to assure better adherence to the treatment program which will result in better overall outcomes.

References:

1. Journal Article - Worcester MU, Murphy BM. Mee VK, Roberts SB, Goble AJ. Cardiac rehabilitation programmes: predictors of non-attendance and drop-out. Eur J Cardiovasc Prev Rehabil. 2004 Aug; 11(4): 328-35.

2. Journal Article - Todaro JF, Biing-Jiun S, Niaura R, Tilemeier PL. Prevalence of depressive disorders in men and women enrolled in cardiac rehabilitation. Journal of Cardiopulmonary Rehabilitation 2005;25:71-75.

NR252 Monday, May 22, 3:00 PM - 5:00 PM

Diagnosing MDD: Are There Better Symptom Criteria Than the *DSM-IV?*

Joseph McGlinchey, Ph.D. *Brown University, Department of Psychiatry and Human Behavior, 235 Plain St., Suite 501, Providence, RI, 02905*, Mark Zimmerman, M.D., Diane D. Young, Ph.D., Iwona Chelminski, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize current and alternative symptom criteria for diagnosing major depressive disorder (MDD), to understand how current and alternative symptoms perform in differentiating MDD cases from non-MDD cases, and to be able to think more critically about the selection of current symptoms used as diagnostic criteria for MDD.

Summary:

Objective: As a chronic and prevalent illness, MDD requires symptom criteria that are able to detect MDD and provide optimal discrimination from non-MDD cases. To date, there is little data available to suggest how well the MDD symptom criteria offered in the latest *Diagnostic and Statistical Manual* (DSM-IV; APA, 1994) achieve these goals, and if there may be alternative symptoms to consider as better diagnostic indicators of MDD relative to those currently suggested in the DSM.

Methods: The Structured Clinical Interview for DSM-IV (SCID) was administered to 1800 treatment-seeking outpatients. Presence or absence of all current DSM symptoms of MDD, as well as alternative depression symptoms (i.e., diminished drive, helplessness, hopelessness, non-reactive mood, psychic and somatic anxiety, subjective and overt anger), was ascertained for each patient. All symptoms were examined in terms of sensitivity, specificity, odds ratios of sensitivity and specificity, and positive and negative predictive values.

Results: Diminished drive exhibited stronger performance in differentiating MDD from non-MDD relative to all currently accepted DSM-IV criteria excepting depressed mood, anhedonia, and diminished concentration/indecisiveness. A compound criteria that combined diminished drive with loss of energy was en-

dorsed by nearly all MDD patients. Helplessness and hopelessness, when combined into a single criterion, performed more strongly than some of the currently accepted DSM-IV criteria. The remainder of alternative symptoms failed to differentiate MDD cases more strongly than current DSM-IV criteria.

Conclusion: Diminished drive, helplessness, and hopelessness may serve as better symptom indicators to consider in diagnosing MDD than many of the current DSM-IV symptoms.

References:

1. Feighner JP, Robins E, Guze SB, Woodruff RA, Winokur G, Munoz R: Diagnostic criteria for usse in psychiatric research. Arch Gen Psychiatry 1972; 26:57-67.
2. Zimmerman M, McGlinchey JB, Young D, Chelminski, I: Diagnosing major depressive disorder: I. A psychometric evaluation of the DSM-IV symptom criteria. J Nerv Dis.

NR253 Monday, May 22, 3:00 PM - 5:00 PM

Using Item Response Theory to Model the Comorbidity of Unipolar Depression and Anxiety Disorder

Joseph B. McGlinchey, Ph.D. *Brown University, Department of Psychiatry and Human Behavior, 235 Plain St., Suite 501, Providence, RI, 02905*, Mark Zimmerman, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to think critically about the controversy over whether current DSM-IV mood and anxiety disorders are best expressed as discrete entities versus dimensionally (i.e., as indicators falling along the continuum of a shared, latent factor). This presentation will also provide an applied example, through full replication of a previous study, of how novel psychometric techniques can provide greater elucidation in our understanding of diagnostic comorbidity.

Summary:

Objective: Comorbidity remains a fundamental challenge in the establishment of a valid nosological system. High rates of comorbidity have been particularly observed amongst unipolar mood and anxiety disorders. This study sought to replicate the findings of a prior study (Krueger & Finger, 2001) that used item response theory (IRT) to model depression and anxiety comorbidity in terms of a shared, latent factor: Internalizing.

Methods: The Structured Clinical Interview for DSM-IV (SCID) was administered to 1800 treatment-seeking outpatients to ascertain the presence or absence of five mood and anxiety disorders: major depression, social phobia, panic disorder/agoraphobia, specific phobia, and GAD. The viability of a single Internalizing factor was tested to account for the covariation between the disorders. Then, a two-parameter logistic (2PL) IRT model examined how the five diagnoses mapped along the continuum of Internalizing. Finally, the Internalizing factor was validated on three, 'real world' indicators of impairment.

Results: Findings were strongly consistent with Krueger and Finger (2001). A confirmatory factor analysis yielded strong evidence for an Internalizing factor underlying the diagnoses (χ^2 = 11.9; CFI = .98; RMSEA = .02). The 2PL model indicated the five diagnoses were representative of the upper half of the Internalizing continuum and were strong discriminators of the factor. Latent trait estimates representing eac

h patient's placement along the Internalizing continuum were robustly associated with current poorer social functioning and time missed from work (p<.001 for each), as well as lifetime hospitalizations (p < .05).

Conclusions: The findings of the current study lend additional support towards an alternative conceptualization of unipolar depression and anxiety disorders. Instead of their current presentation in the *DSM-IV* as representing discrete diagnostic entities, these common mood and anxiety disorders may be re-envisioned as higher-end indicators of a common factor that is associated with real social cost.

References:

1. Krueger RF, Finger MS: Using item response theory to understand comorbidity among anxiety and unipolar mood disorders. Psychol Assess 2001; 13:140-151.
2. Mineka S, Watson D, Clark LA: Comorbidity of anxiety and unipolar mood disorders. Annu Rev Psychol 1998; 49:377-412.

NR254 Monday, May 22, 3:00 PM - 5:00 PM

Quetiapine Augmentation of SSRIs/SNRIs in Major Depression With Anxiety

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Educational Objectives:

At the conclusion of this presentation, the participant should understand the benefits of using quetiapine to augment SSRI/SNRI therapy in patients with depression and anxiety.

Summary:

Objective: Atypical antipsychotics may be effective in treating major depression.[12] This double-blind, randomized study evaluated quetiapine augmentation of SSRIs/SNRIs for major depression with residual depressive and prominent anxiety symptoms.

Methods: Fifty-eight patients with residual symptoms following ≥6 weeks SSRI/SNRI treatment (HAM D ≥18; HAM-A ≥14) received quetiapine (50 600 mg/day) or placebo for 8 weeks. Primary efficacy endpoint: mean change (baseline to Week 8 [LOCF]) in HAM D and HAM-A. Secondary endpoints: CGI Severity; Global Assessment Scale (GAS); incidence of AEs.

Results: 18/29 quetiapine-treated (mean dose: 202±93 mg/day) and 16/29 placebo-treated patients completed the study. Significant improvements (quetiapine versus placebo) were seen at Weeks 1 (p≤0.01) and 8 (p≤0.01) for HAM-D (-6.5, -11.2 versus -2.9, -5.5); HAM A (-7.4, -12.5 versus -3.4, -5.9); CGI Severity (-0.45, -1.5 versus -0.07, -0.6); GAS (+5.7, +17.5 versus +1.7, +6.6). Overall, 7/17 HAM-D and 6/14 HAM-A items were improved with quetiapine (p<0.05 versus placebo at Week 8). Main reasons for discontinuation: AEs for quetiapine (n=8); inefficacy for placebo (n=9). Most common AEs (quetiapine versus placebo): sedation/somnolence/lethargy (n=25 versus n=14); dry mouth (n=13 versus n=4); weight gain (n=12 versus n=5).

Conclusions: Quetiapine combined with SSRIs/SNRIs improved residual depressive and anxiety symptoms in major depression; tolerability was consistent with previous quetiapine studies.

References

1. Kennedy SH, Lam RW: Enhancing outcomes in the management of treatment resistant depression: a focus on atypical antipsychotics. Bipolar Disord 2003; 5 (Suppl 2):36-47

2. Yargic LI, Corapcioglu A, Kocabasoglu N, Extended Release dogan A, Koroglu G, Yilmaz D: A prospective randomized single-blind, multicenter trial comparing the efficacy and safety of paroxetine with and without quetiapine therapy in depression associated with anxiety. Int J Psychiatry Clin Pract 2004; 8:205 211

References:

1. 1. Kennedy SH, Lam RW: Enhancing outcomes in the management of treatment resistant depression: a focus on atypical antipsychotics. Bipolar Disord 2003; 5 (Suppl 2):36-47.
2. 2. Yargic LI, Corapcioglu A, Kocabasoglu N, Erdogan A, Koroglu G, Yilmaz D: A prospective randomized single-blind, multicenter trial comparing the efficacy and safety of paroxetine

with and without quetiapine therapy in depression associated with anx.

NR255 Monday, May 22, 3:00 PM - 5:00 PM

Improving Outcomes in Depression: A Focus on Somatic Symptoms

Roger S. McIntyre, M.D. *University Health Network, Mood Disorders Psychopharmacology Unit, 399 Bathurst Street, MP-9-325, Toronto, ON, M5T 2S8, Canada*, Jakub Z. Konarski, M.S.C., Deborah A. Mancini, M.A., Mateusz Zurowski, M.D., Peter Giacobbe, M.D., Joanna K. Soczynska, B.S.C., Sidney H. Kennedy, M.D.

Educational Objectives:

The primary aim of this investigation was to describe the relationship between the alleviation of somatic symptoms and improvement in overall depression outcome in patients receiving antidepressant therapy in primary-care settings.

Summary:

Background: It is hypothesized that somatic symptom alleviation is a significant predictor of overall outcome in depressed primary-care patients.

Method: Depressed primary-care patients (n=205) meeting DSM-IV-TR criteria received open-label antidepressant therapy. The HAMD-17 was the primary symptom-measurement tool, with the MADRS and CGI-I/S as secondary measures. As a proxy for somatic symptoms, eight items from the HAMD-17 (HAMD-S) and three items from the MADRS (MADRS-S) which measure somatic symptoms were identified and extracted.

Results: There was a significant correlation between improvement on the HAMD-S and overall reduction on MADRS total score ($r=0.766$, $p<0.001$), response ($r=0.594$, $p<0.001$) and remission ($r=0.552$, $p<0.001$) respectively. Improvement on the MADRS-S also correlated with overall HAMD-17 improvement ($r=0.782$, $p<0.001$), along with response ($r=0.649$, $p<0.001$) and remission rates($r=0.539$, $p<0.001$), respectively. Both HAMD-S and MADRS-S correlated with global improvement as measured by CGI-I/S ($p<0.001$).

Conclusions: A reciprocal interaction between somatic symptoms and other depressive-symptom domains is implied by this analysis. Clinicians are encouraged to identify, track, and target the somatic symptoms of depressive illness

References:

1. Fava M: Somatic symptoms, depression, and antidepressant treatment. J Clin Psychiatry 2002; 63(4):305-307.
2. Paykel ES, Ramana R, Cooper Z, Hayhurst H, Kerr J, Barocka A: Residual symptoms after partial remission: an important outcome in depression. Psychol Med 1995; 25(6):1171-1180.

NR256 Monday, May 22, 3:00 PM - 5:00 PM

Anxious Residual Symptoms in Depressed Primary Care Patients

Roger S. McIntyre, M.D. *University Health Network, Mood Disorders Psychopharmacology Unit, 399 Bathurst Street, MP-9-325, Toronto, ON, M5T 2S8, Canada*, Jakub Z. Konarski, M.S.C., Sidney H. Kennedy, M.D.

Educational Objectives:

To evaluate the relationship between anxiety symptoms and depressive symptom severity, chronicity of illness course, and poor outcome.

To characterize the burden of anxiety amongst residual depressive symptoms in naturalistic primary-care settings.

Summary:

Background: Symptomatic remission is the optimal outcome in depression. We aimed to characterize the burden of anxiety amongst residual depressive symptoms in naturalistic primary-care settings.

Method: A post-hoc analysis of a database comprised of naturalistically-treated depressed patients receiving treatment across Canada. This bilingual (English and French), multicenter, randomized validation study was conducted in forty-seven primary-care settings in four provinces of Canada. Patients who met Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text-Revision (DSM-IV-TR) criteria for a major depressive episode, in the context of a MDD (n=454) were enrolled. Eligible patients received open-label, flexible-dose antidepressant treatment. Patients with at least one post-baseline assessment were considered evaluable. We derived a composite anxiety score which served as a proxy of the anxiety burden (expressed as an anxiety ratio). Correlations between the baseline and endpoint anxiety ratio and overall response/remission status were conducted.

Results: The composite anxiety ratio at baseline did not correlate with the probability of remitting at endpoint ($p=0.534$). After eight weeks of antidepressant therapy remitting patients evinced a statistically significant decrease in the anxiety ratio ($p=0.041$). Moreover, an inverse correlation was noted between endpoint anxiety symptom severity and probability of remission ($p=0.026$). The burden of anxiety, presented as the anxiety ratio, was higher in nonremitting patients at endpoint ($p=0.828$).

Conclusion: Residual depressive symptoms represent ongoing illness activity in depression. Anxiety symptoms are disproportionately represented amongst residual symptoms. Sharpening the focus of therapeutic interventions in the clinical environments calls for tracking and managing residual anxiety symptoms.

References:

1. Nierenberg AA, Keefe BR, Leslie VC, Alpert JE, Pava JA, Worthington JJ, III, Rosenbaum JF, Fava M: Residual symptoms in depressed patients who respond acutely to fluoxetine. J Clin Psychiatry 1999; 60(4):221-225.
2. Paykel ES, Ramana R, Cooper Z, Hayhurst H, Kerr J, Barocka A: Residual symptoms after partial remission: an important outcome in depression. Psychol Med 1995; 25(6):1171-1180.

NR257 Monday, May 22, 3:00 PM - 5:00 PM

Diagnosing Bipolar Disorder Amongst Pseudo Unipolar Patients Referred to an Outpatient Mood Clinic

Roger S. McIntyre, M.D. *University Health Network, Mood Disorders Psychopharmacology Unit, 399 Bathurst Street, Toronto, ON, M5T 2S8, Canada*, Deborah Mancini, M.A., Joanna K. Soczynska, B.S.C., Jakub Z. Konarski, M.S.C., Chris Lam, Sidney H. Kennedy, M.D.

Educational Objectives:

To estimate the proportion of persons with a history of treatment resistant or chronic depression who are diagnosed as having bipolar disorder.

Summary:

Background: There is an increasing appreciation of the prevalence of bipolar spectrum disorder in the general population and in the health care setting. Several reports indicate that up to 20-40% of all 'unipolar' patients are in fact 'pseudounipolar'. We aim to estimate the proportion of persons with a history of treatment

resistant or chronic depression who are diagnosed as having bipolar disorder.

Method: Consecutive adult patients (18-65 years) attending the Mood Disorders Psychopharmacology Unit (MDPU), University Health Network, University of Toronto, from October 2001 to November 2005, were evaluated with a retrospective chart review.

Results: Of 1000 patients referred to the MDPU, the diagnostic breakdown was as follows: MDD (n=518, 51%); Bipolar Disorder (BD) (n=381, 38%); Anxiety Disorders (n=18, 2%), other diagnoses (n=101, 10%). Of the patients who were initially referred to the MDPU with a working diagnosis of MDD, 16% (n=181) were diagnosed by the MDPU with BD. Several sociodemographic and treatment variables were associated with a diagnosis of BD, which will be presented.

Conclusion: A substantial proportion of patients referred to a tertiary mood disorders program with chronic or treatment resistant depression may have an occult diagnosis of bipolar disorder. All patients with a diagnosis of MDD should be carefully screened for bipolar disorder and repeatedly over the course of their illness. Treatment resistant depression and/or chronic depressed patients should be particularly screened for subtler expressions for bipolar disorder.

References:

1. Goldberg, J. F., Harrow, M., & Whiteside, J. E. (2001). Risk for bipolar illness in patients initially hospitalized for unipolar depression. Am.J.Psychiatry, 158, 1265-1270.
2. Sharma, V., Khan, M., & Smith, A. (2005). A closer look at treatment resistant depression: is it due to a bipolar diathesis? J.Affect.Disord., 84, 251-257.

NR258 Monday, May 22, 3:00 PM - 5:00 PM

Childhood Physical and Sexual Abuse Predicts Suicidality in Adult Bipolar Disorder

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Educational Objectives:

To evaluate the effect of childhood sexual and physical abuse on suicidality and other indices of illness severity in adult bipolars.

Summary:

Objectives: Bipolar disorder is a prevalent, severe and disabling illness. Psychosocial stressors are reported to affect the course and outcome of bipolar disorder, particularly early in the illness course. Adverse childhood experiences are a non-specific risk factor for disparate psychiatric disorders and may be a moderator of a more severe bipolar course. Preliminary data suggests that childhood physical and sexual abuse is associated with suicidality in adult bipolar disorder. We aimed to evaluate the effect of childhood sexual and physical abuse on suicidality and other indices of illness severity in adult bipolars.

Method: Adult outpatients (N=1000) seen at the Mood Disorders Psychopharmacology Unit (MDPU), University Health Network, University of Toronto, from October 2001 to November 2005 were evaluated with a retrospective chart review.

Results: Patients with bipolar disorders (n=318) frequently reported a history of physical and sexual abuse (n=81, 44%). The self-reported childhood sexual and physical abuse was associated with suicidality in adults with bipolar disorder (n=52, 54%; p= 0.03) and with other indices of bipolar severity (i.e. at least one hospitalization; n=39, 26.2%, p=0.004).

Conclusions: The data herein suggests that distal stressors (e.g. childhood sexual and physical abuse) are an adverse prognosticator in bipolar disorder and are associated with suicidality. Risk assessment in bipolar disorder should include inquiry into past history of physical and sexual trauma.

References:

1. Brown, G. R., McBride, L., Bauer, M. S., & Williford, W. O. (2005). Impact of childhood abuse on the course of bipolar disorder: A replication study in U.S. veterans. J.Affect.Disord..
2. Leverich, G. S., Altshuler, L. L., Frye, M. A., Suppes, T., Keck, P. E., Jr., McElroy, S. L. et al. (2003). Factors associated with suicide attempts in 648 patients with bipolar disorder in the Stanley Foundation Bipolar Network. J.Clin.Psychiatry, 6.

NR259 Monday, May 22, 3:00 PM - 5:00 PM

OREON 2: Factors Influencing Remission Rates in Depression

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Educational Objectives:

The OREON 2 observational study of remission in depressed patients treated in primary care and in patients treated by psychiatrists analyzed risk factors associated with low remission rates. The data shown provide sociodemographic as well as diagnostic and treatment factors that affect remission rates. The data will help physicians identify depressed patients at risk for low remission rates and identify diagnostic and treatment factors that are associated with improved remission.

Summary:

Objective: OREON 2 (Objective Remission in Depression) studied remission rates as well as patient-related factors affecting remission in depressed patients treated after the participation of their treating physician to an internet based interactive educational intervention

Method: In this observational study, investigators each included 10 consecutive patients with newly diagnosed depression. At the start of treatment, socio-demographic parameters, method of diagnosis, disease severity and history were recorded. Patients completed the Physicians Health Questionnaire (PHQ), the Sheehan Disability Scale (SDS) and the Carroll scale. Symptom severity was assessed using the HAM-D 7 (GPs) or the HAMD-17 (psychiatrists) .

During a routine follow up after 3 to 6 months of treatment, HAM-D scales, PHQ, Carroll and SDS were rated. Treatment history, and compliance were also recorded.

Results: 200 GP's and 20 psychiatrists screened a total of 1800 patients. Overall remission was 50% in primary care and 40% in specialized care. The prevalence of remission will be shown according to various cofactors: gender, age, region, socio-economic status, severity and duration of disease, co-morbidities as well as treatment and compliance. Conclusion: OREON 2 provides cofactors affecting remission rates and helps physicians identifying depressed patients at risk for not reaching remission.

The OREON project is funded by Wyeth Pharmaceuticals Belgium

References:

1. Keller, MB, 2003. Past, present and future directions for defining optimal treatment outcome in depression. Remission and Beyond. JAMA, 289: pp. 3152-3160.
2. McIntyre, R., Kennedy, S., Bagby, M., Bakish, D., 2002. Assessing full remission. J Psychiatry Neurosci ;27(4): pp. 235-9.

NR260 Monday, May 22, 3:00 PM - 5:00 PM

The Role of Duration of Untreated Illness on the Outcome of MDD

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the role of the duration of untreated illness (DUI), defined as the time elapsing between the onset of Major Depressive Disorder (MDD) and the first adequate antidepressant treatment, on the long-term outcome of MDD.

Summary:

Objective: The aim of this study was to investigate the role of the duration of untreated illness (DUI), defined as the time elapsing between the onset of MDD and the first adequate antidepressant treatment, on the long-term outcome of MDD. *Methods*: 113 DSM-IV-TR MDD patients, who gave their informed consent, were the sample studied. Patients were sub-divided into two groups, with DUI < 1 year (N=75) and with DUI > 1 year (N=38). The main demographic, clinical, and outcome variables were compared between the two patient groups (Student's t-tests or chi-square tests).

Results: Patients with DUI> 1 year had a significantly higher number of Major Depressive Episodes lifetime (t=2.045, p<0.02). No significant differences between the two groups were found with respect to the other variables considered, including the frequency of comorbidity with onset later than MDD, the number of hospitalizations, and the development of rapid cycling course. *Conclusions:* Results from this study suggest that the DUI can negatively influence the outcome of DDM. These results will be discussed also considering data from studies on the impact of DUI on other mood disorders, i.e., Bipolar Disorder.

References:

1. Craig TJ, Bromet EJ, Fennig S, Tanenberg-Karant M, Lavelle J, Galambos N. Is there an association between duration of untreated psychosis and 24-month clinical outcome in a first-admission series? Am J Psychiatry 157: 60-66; 2000.
2. Mundo E, Santini A, Salvadori D, Altamura AC. Is duration of untreated illness (DUI) a risk factor of poor outcome in Bipolar Disorder? Presented at the 158th Annual Meeting of the American Psychiatric Association, Altanta (Georgia), May 21-26 2005.

NR261 Monday, May 22, 3:00 PM - 5:00 PM

Prediction of Response to Lamotrigine and Placebo for Bipolar Depression: A Clinically Useful Probability Analysis

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Educational Objectives:

At the conclusion of this presentation, the participant should be able understand patient response and tolerability to lamotrigine treatment.

Summary:

Objectives: Lamotrigine is frequently prescribed for patients with bipolar depression.[1,2] This is the first study that examines the probability of response at the end of a trial of lamotrigine by week for the treatment of bipolar depression.

Methods: Data were pooled from 3 randomized placebo-controlled studies that included 579 patients with bipolar I or II disorder and who had a major depressive episode. Full response was defined as > 50% decrease in HAMD-17 without emergence of mania or hypomania. Conditional probability of response at 7 weeks was calculated for minimal (<30% improvement), partial (30-49% improvement), and full response at weeks 1 through 6.

Results: The majority of patients with a full response at each week were also full responders at the end of the trial (75-90%) in both the placebo and lamotrigine treatment groups with a generally higher proportion of lamotrigine treated patients responding. A greater number of lamotrigine treated patients with partial response at each week (37%-76%) compared to placebo treated patients (18%-48%) were also full responders at the end of the trial. Lamotrigine treated patients with minimal response at weeks 1, 2, 3, 4, 5, and 6 were less likely to be full responders by week 7 with 53%, 43%, 38%, 24%, 27%, and 11% respectively.

Conclusions: As minimal response persisted, patients had a declining probability of final response. Those with partial and full response at each time point were more likely to continue as responders by the end of the trial.

This study was supported by GlaxoSmithKline.

References:

1. Suppes T, Kelly DI, Perla JM: Challenges in the management of bipolar depression. J Clin Psychiatry 2005; 66 Suppl 5:11-16.
2. Bhagwager Z, Goodwin GM: Lamotrigine in the treatment of bipolar disorder. Expert Opin. Parmacotherapy 2005; 6(8):1401-1408.

NR262 Monday, May 22, 3:00 PM - 5:00 PM

A Five-Year Retrospective Study in Schizobipolar Disorder Outpatients

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that schizobipolar disorder patients have demographic, clinical and therapeutic features similar to bipolar I patients and the data support its definite inclusion in the bipolar spectrum group.

Summary:

Background: Schizobipolar disorder is considered related to both schizophrenia and bipolar disorder. We aimed to describe with retrospective methodology the demographic, clinical, and treatment features in a group of schizobipolar disorder patients who have been treated for at least a 5-year period and compare them with bipolar I and schizophrenic patients who were treated during the same period. Method: We compared the demographic and clinical data of 61 schizobipolar, 57 bipolar I, and 55 schizophrenic outpatients who were diagnosed and treated for at least 5 years in the outpatient clinic in the Federal University of Rio de Janeiro. Results: The schizobipolar disorder patients had a profile similar to the bipolar I patients but are significantly different from schizophrenic patients in educational level, marital status, occupation, drug and alcohol abuse episodes, presence of depressive, mixed and maniac episodes, family history of bipolar I and mood disorders, and use of medications. Only the age of onset, suicide

attempts, and family history of suicide are not significantly different among the groups. The schizophrenic patients used antipsychotics for more days and the schizobipolar and bipolar I used more antidepressants and mood stabilizers. 37 (60.6%) schizobipolar patients had their diagnosis changed to bipolar disorder by their physician in different periods during the period studied. Limitations: It is a retrospective data description based on a naturalistic treatment. The family history was collected from the patient and whenever possible from one first-degree relative.

References:

1. Akiskal HS, Bourgeois ML, Angst J, Post R, Moller H, Hirschfeld R. Re-evaluating the prevalence of and diagnostic composition within the broad clinical spectrum of bipolar disorders. J Affect Disord 2000; 59: S5'S30.
2. Slama F, Bellivier F, Henry C, Rousseva A, Etain B, Rouillon F, Leboyer M. Bipolar patients with suicidal behavior: toward the identification of a clinical subgroup. J Clin Psychiatry 2004; 65: 1035' 1039.

NR263 Monday, May 22, 3:00 PM - 5:00 PM

Onset of Antidepressant Action and Acute Efficacy and Safety of Duloxetine Versus Escitalopram and Placebo in the Treatment of MDD

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the comparative onset of efficacy as well as the efficacy and tolerability of duloxetine and escitalopram in the acute treatment of depression.

Summary:

Objective: To compare onset of efficacy (OE) and acute phase efficacy and safety outcomes of duloxetine with the 5HT-specific uptake inhibitor escitalopram.

Methods: Adult patients (N=684) with MDD were randomized to duloxetine 60mg once daily (QD; n=273), escitalopram 10mg QD (n=274), or placebo QD (n=137) for 8 weeks. OE was defined a priori as at least a 20% decrease from baseline in the 17-item Hamilton Rating Scale for Depression ($HAMD_{17}$) Maier subscale that was maintained at each visit.

Results: The probability of meeting OE criteria at Week 2 for duloxetine- and escitalopram-treated patients was estimated as 42.6% versus 35.2%, respectively (p=.097). Placebo-treated patients met OE criteria (21.5%) at a significantly lower rate than duloxetine (p<.001) or escitalopram (p=.008). Secondary analyses found probabilities of response for placebo, duloxetine, and escitalopram were 36.9%, 48.7%, and 45.3%, and for remission 27.7%, 40.1%, and 33.0%, respectively, with no significant differences between groups. Mean change in total $HAMD_{17}$ scores were -5.97, -7.61, and -7.22, respectively with only duloxetine significantly different from placebo (p=.021). Both antidepressants had statistically significant changes in CGI-S and PGI-I when compared with placebo. The discontinuation rate due to adverse events was similar for each group (placebo 5.8%, duloxetine 7.3%, escitalopram 5.1%). Treatment-emergent adverse events occurring significantly more frequently among duloxetine-treated patients, when compared with those receiving escitalopram, were nausea, dry mouth, vomiting, yawning, and irritability. **Conclusions**: In this study, duloxetine 60mg QD had onset of sustained clinically meaningful improvement that was at least as fast as escitalopram 10mg QD. The proportion of remitters and responders treated with placebo, duloxetine, and escitalopram was not significantly different at 8 weeks. However, duloxetine showed significant differences from placebo on the HAMD17 while escitalopram did not. Most other measures found similar changes with duloxetine and escitalopram. Funding provided by Eli Lilly and Company.

References:

1. Hirschfeld RM, et al. Time course of depression-symptom improvement during treatment with duloxetine. Depress Anxiety. 2005;21(4):170-7.
2. Bielski RJ, et al. A double-blind comparison of escitalopram and venlafaxine extended release in the treatment of major depressive disorder. J Clin Psychiatry. 2004 Sep;65(9):1190-6.

NR264 Monday, May 22, 3:00 PM - 5:00 PM

Effects of Sildenafil Citrate Treatment on Ejaculatory/ Orgasm Delay and Erectile Dysfunction in Serotonergic, Antidepressant-Associated Sexual Dysfunction

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Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the need for effective treatment of serotonergic reuptake inhibitor-associated ejaculatory delay and erectile dysfunction and the complicated relationship between the two.

Summary:

Objective: Serotonergic reuptake inhibitor antidepressant-associated sexual dysfunction (SRI-AASD) is complex, involving primarily disordered orgasm and Extended Release ectile dysfunction (ED) in men. Although controlled trials of sildenafil have demonstrated efficacy for treatment of ED due to various etiologies, including Sustained Release I-antidepressants, its effectiveness for ejaculatory delay (EJD) and orgasm delay is unclear. This report examines sildenafil treatment for Sustained Release I-AASD with a focus on ED, EJD, and their concurrence.

Methods: 90 men with MDD in remission, on stable-dose antidepressant, and Sustained Release I-AASD were randomized to receive sildenafil (flexible dose, 50 mg or 100 mg) or placebo for 6 weeks. Subjects entered an open-label extension phase where they received sildenafil for 18 additional weeks. Outcome measures included the International Index of Extended Release ectile Function, University of New Mexico-Sexual Function Inventory, Clinical Global Impression-Sexual Function (CGI-SF), and Hamilton Depression scales (HAM-D).

Results: ED (87%) and EJD (70%) were highly prevalent. Sildenafil treatment resulted in significant improvement in sexual dysfunction domain scores for both double-blind and open-label phases of the 24-week study (effect size=1.07, 95% CI, 0.77-1.37); HAM-D remained ≤7, without depression relapses or recurrences. Placebo response rates were <5%. Full response rates (CGI=1) were 76.5% for ED without EJD, 40.5% for ED with EJD, 14.3% for EJD without ED, 50.9% for total ED, and 40.5% for total EJD (P=0.02).

Conclusions: Sustained Release I-AASD involves multiple sexual dysfunctions. Sildenafil treatment of ED appears to be attenuated in association with EJD whereas associated ED enhanced the response to EJD. The ED-EJD relationship is complex as to whether the concurrence reflects cause-effect, forme-fruste, common diathesis, complications, independent-interactive, or severity of conditions, and to what extent phosphodiesterase inhibitor agents are of primary or secondary benefit.

References:

1. HG, Hensley PL: Selective phosphodiesterase type-5 inhibitor treatment of serotonergic reuptake inhibitor antidepressant-associated sexual dysfunction: a review of diagnosis, treatment, and relevance. CNS Spectr 2003; 8:194-202.

2. Nurnberg HG, Hensley PL, Gelenberg AJ, Fava M, Lauriello J, Paine S: Treatment of antidepressant-associated sexual dysfunction with sildenafil: a randomized controlled trial. JAMA 2003; 289:56-64.

NR265 Monday, May 22, 3:00 PM - 5:00 PM

Major Depression, Somatic Pain, and Health Care Costs in an Urban Primary Care Practice

Mark Olfson, M.D. *Columbia University, Psychiatry, 1051 Riverside Drive, New York, NY, 10032*, Marc J. Gameroff, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to describe relationships between major depressive disorder, pain-related interference in daily function, and health care costs in an urban primary care practice.

Summary:

Background: Depression is associated with somatic pain and a substantial elevation of general medical care costs.

Objective: To evaluate the extent to which pain related interference in daily function contributes to the total medical care costs of primary care patients with MDD.

Methods: A systematic sample of primary care patients (n= 1,028) from an urban practice were assessed with the PRIME-MD PHQ, Sheehan Disability Scale, a medical illness checklist, and the SF-12, which includes a pain-related functional interference item. Medical charges for inpatient, outpatient, and emergency department services were assessed for the 6 month period preceding and following the index medical visit. Patients with and without MDD were first compared with respect to predicted mean medical care costs and pain-related interference. Predicted mean medical care costs of MDD patients with little or no pain related interference were then compared to those with moderate or more severe pain related interference in daily function.

Results: As compared to patients without MDD (n=821), those with MDD (n=207) had significantly higher predicted mean medical care costs ($19,838 versus $6,268, t = 14.9, $p < .0001$), after controlling for age and sex, and were significantly more likely to report at least moderate pain related interference in daily function (MDD: 69.1% versus no MDD: 38.5%, χ^2=61.3, df=1, p<.0001). Predicted mean medical care costs of patients with MDD and at least moderate pain were on average 2.33 times (95% confidence interval, 1.34-4.05) as high as patients with MDD and little or no pain related interference.

Conclusions: In this primary care practice, pain makes an important contribution to the total health care costs of patients with MDD.

References:

1. Katon WJ, Lin E, Russo J, Unutzer J: Increased medical costs of a population-based sample of depressed elderly patients. Arch Gen Psychiatry 2003;60:897-903.

2. Katon WJ: Clinical and health services relationships between major depression, depressive symptoms, and general medical illness. Biol Psychiatry 2003;54:216-226.

NR266 Monday, May 22, 3:00 PM - 5:00 PM

The Association Between Smoking, Suicidality, and Clinical Course in Bipolar Disorder

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that a history of smoking in subjects with bipolar disorder is associated with worse course, greater illness burden, anxiety and substance use disorder comorbidity, and history of a suicide attempt.

Summary:

Objective:

The purpose of this study was to assess the relationship between smoking and bipolar disorder.

Methods:

399 outpatients with bipolar disorder were evaluated with the Affective Disorders Evaluation (ADE), a validated, semi-structured interview, and the Mini International Neuropsychiatric Interview (MINI).

Results:

38.8% of subjects had a history of smoking. Having ever smoked was associated with earlier age of onset of first depressive episode (15.7 versus 18.2 years, p=0.004), earlier age of onset of first manic episode (19.7 versus 22.4 years, p=0.013), lower Global Assessment of Functioning (GAF) at the time of entry to the clinic (56.1 versus 59.1, p=0.003), higher Clinical Global Impressions for Bipolar Disorder (CGI-BP) at the time of entry to the clinic (3.1 versus 2.8, p=0.015), a history of a comorbid anxiety disorder, (68% versus 53.4%, p<. 01), a history of alcohol use disorders (56.7% versus 30.5%, p<0.001), a history of substance use disorders (43.3 % versus 20.3%, p<0.001), and having made a suicide attempt (47% versus 25%, OR 2.74, 95% C.I. 1.77-4.23). After controlling for these factors in a binary logistic regression model, a significant association persisted between smoking and suicide attempts (OR 2.3, 95% C.I. 1.36-3.93. p=0.002) and between smoking and substance use disorders (OR 2.1, 95% C.I. 1.16-3.90, p=0.15).

Conclusions:

A history of smoking is highly prevalent in subjects with bipolar disorder, and is associated with worse course, greater illness burden, anxiety and substance use disorder comorbidity, and history of a suicide attempt. The strong relationship between nicotine use and bipolar disorder, including its relationship with suicidality, merits further exploration.

References:

1. Gonzalez-Pinto A, Gutierrez M, et al: Tobacco smoking and bipolar disorder. J Clin Psychiatry 1998; 59(5):225-8.

2. Oquendo MA, Galfalvy H, et al: Prospective study of clinical predictors of suicidal acts after a major depressive episode in patients with major depressive disorder or bipolar disorder. Am J Psychiatry 2004; 161(8): 1433-41.

NR267 Monday, May 22, 3:00 PM - 5:00 PM

Adjunctive Risperidone in the Treatment of GAD: A Double-Blind, Placebo-Controlled, Randomized Study

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Kosik-Gonzalez, M.A., Ibrahim Turkoz, M.S., Mary Kujawa, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to (1) identify residual symptoms that are rated as most troubling by patients with GAD, (2) evaluate a potentially useful instrument for assessing treatment outcomes in patients with GAD, and (3) assess the efficacy of treatment with risperidone in patients with residual symptoms.

Summary:

Background: Residual symptoms remain refractory in a considerable proportion of patients with GAD. This study examined the effectiveness of risperidone compared with placebo added to standard care in GAD patients.

Methods: The subjects, patients with a DSM-IV GAD diagnosis who remained symptomatic despite treatment with an anxiolytic agent for ≥8 weeks, received adjunctive risperidone or adjunctive placebo for 6 weeks. The primary effectiveness measure was the patient-rated Most Troubling Symptoms (MTS) scale, comprised of 7 GAD symptoms from the DSM-IV rated on a scale of 0-10 via a telephone interactive voice response system (Healthcare Technology Systems). The primary endpoint was the MTS total score (sum of the 4 items identified as most troubling by each patient at baseline) at the week-4 endpoint (LOCF).

Results: 390 patients comprised the intent-to-treat population (risperidone n=196, placebo n=194). The mean (± SD) modal dose of risperidone was 0.9±0.2 mg/day over weeks 1-4. The 4 MTS items rated most often by patients as most troubling were excessive anxiety or worry (76%), feeling restless (68%), trouble sleeping (66%), and getting tired easily (55%). Greater improvements in MTS total scores were seen with adjunctive risperidone than adjunctive placebo, with significant ($P < 0.05$) differences at week 1 but not at endpoint. On the Patient-Rated Global Improvement Scale, significantly greater improvements were seen at weeks 1 and 3 and at endpoint in patients receiving risperidone compared with placebo ($P<0.05$). Significantly greater satisfaction with medication and life (Q-LES-Q scores) was reported by patients receiving risperidone than placebo.

Conclusions: Preliminary evidence of the efficacy of adjunctive risperidone on residual symptoms in GAD patients was observed. The patient-rated MTS appears to be a useful instrument for assessing treatment effects in GAD patients. Supported by Janssen, L.P.

References:

1. Rynn MA, Brawman-Mintzer O. Generalized anxiety disorder: acute and chronic treatment. CNS Spectr 2004;9:716-723.
2. Gorman JM. Treating generalized anxiety disorder. J Clin Psychiatry 2003;64(suppl 2):24-29.

NR268 Monday, May 22, 3:00 PM - 5:00 PM

Duloxetine Alone Versus Duloxetine Plus Non-Pharmacological Intervention in the Treatment of Depression: Does the Addition of a Telephone Intervention Improve Antidepressant Outcomes?

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that the use of a non-pharmacological intervention in concert with optimized antidepressant treatment may not necessarily confer additional benefits during acute treatment of MDD.

Summary:

Objective: There is increasing recognition that non-adherence and discontinuation limit the effectiveness of pharmacological interventions for depression. We hypothesized that combining a standardized telephone adherence support intervention with an antidepressant (duloxetine) would lead to superior outcomes in the treatment of depressed patients compared with antidepressant alone.

Method: Depressed adults were randomized to receive duloxetine 60-120 mg/day alone or duloxetine 60-120 mg/day plus telephone intervention for 12 weeks of open-label treatment. The primary outcome measure was the percentage of patients in remission (endpoint $HAMD_{17}$ total score ≤7). Additional efficacy measures included response rates (≥50% decrease in $HAMD_{17}$ total score). Safety and tolerability were assessed via reporting of treatment-emergent adverse events (TEAEs), vital signs and laboratory analytes. The telephone intervention was based upon relevant health psychology theory, and designed to improve treatment adherence and reduce study discontinuation. It was delivered to patients via telephone calls occurring approximately 1, 4, and 9 weeks after initiation of duloxetine treatment.

Results: 962 patients were enrolled. No significant baseline differences were observed between treatment groups. Remission rates (42. 8% versus 43.5%) and response rates (56.6% versus 58. 4%) were similar between duloxetine alone and duloxetine plus telephone intervention groups. A similar proportion of patients in each treatment group completed the study, and adverse event discontinuation rates were not significantly different (10.7% versus 13.0%). TEAEs were more common in the telephone intervention group, although only constipation (3.5% versus 10.1%) and hot flushes (0.2% versus 1.7%) were reported significantly more frequently. Adherence to drug treatment was high in both treatment groups.

Conclusions: Use of a telephone intervention in combination with duloxetine did not appear to improve depression outcomes compared with duloxetine alone (perhaps due to the high drug adherence in both treatment groups which was likely due to study procedures), but was associated with increased TEAE reporting.

References:

1. McDonald HP, Garg AX, Haynes RB. 2002. Interventions to enhance patient adherence to medication prescriptions ' scientific review. JAMA 288:2868-2879.
2. Nemeroff CB, Schatzberg AF, Goldstein DJ, Detke MJ, Mallinckrodt C, Lu Y, Tran PV. 2002. Duloxetine for the treatment of major depressive disorder. Psychopharmacology Bulletin 36:106-132.

NR269 Monday, May 22, 3:00 PM - 5:00 PM

Frontal EEG at One Week Predicts Response toTreatment With Citalopram in MDD

Russell E. Poland, Ph.D. *Cedars-Sinai Medical Center, 8730 Alden Drive, E-123, Los Angeles, CA, 90048*, Scott D. Greenwald, Ph.D., Charles P. Smith, B.S., Christina Kustak, M.S.N., Julie Schulz, B.S., Sarah Rowe, B.S., Lev Gertsik, M.D.

Educational Objectives:

To investigate the performance of automated EEG analysis as a clinically useful indicator of treatment efficacy in major depressive disorder.

Summary:

Objective: To investigate the performance of automated EEG analysis as a predictor of response to citalopram treatment in patients with MDD.

Method: Following IRB approval, 26 subjects (mean age 41.0 + 9.8; 42.3 % female) meeting DSM-IV criteria for MDD with baseline HAM-D ≥ 17 entered an 8-week treatment trial with citalopram. Doseage began at 20mg/day and was increased at the physician's discretion to 40mg/day after week 4 and 60mg/day after week 6. HAM-D and 4-channel EEGs (F7-Fpz, F8-Fpz, A1-Fpz, A2-Fpz) were recorded at baseline, week 1, 2, 4, and 8. Positive treatment response was defined as a reduction in HAM-D at week 8 > 50%. An EEG index [Bis-Dep (rev 0.2)] was developed to predict treatment response using EEGs recorded at baseline and week 1.

Results: 14 patients (54%) responded to citalopram treatment. The EEG index predicted response with 81% accuracy (n=26). As anticipated, the predictive accuracy was higher in the 8 subjects whose dosage remained constant following the EEG assessments used to make the prediction compared to the 18 subjects who received some adjustment after week 1 (i.e., 88% versus 78%, p >0.05).

Discussion: EEG response early in the course of citalopram treament is predictive of clinical efficacy measured at 8 weeks. Supposedly, the ability of the EEG index to predict response in patients with doseage increases might be improved by measuring EEG responses 1 week after each dose increase. This hypothesis is currently being tested in a prospective evaluation of this index in a large, multi-center trial.

Conclusion: Using assessments at baseline and week 1, the EEG index predicted clinical response to citalopram treatment. The predictive performance of the index was better in subjects with no doseage changes after the final EEG assessment used to make the prediction.

References:

1. Cook IA, et al: Early Changes in Prefrontal Activity Characterize Clinical Responders to Antidepressants. Neuropsychopharmacology 2002; 27:130-131.
2. Poland R, et al: Change in Frontal EEG Predicts Response to Citalopram Treatment in MDD. 2005 APA Annual Meeting (#541).

NR270 Monday, May 22, 3:00 PM - 5:00 PM

Efficacy of Duloxetine Versus Placebo in Mild, Moderate, and More Severely Ill Patients With MDD

Apurva Prakash, B.S. *Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN, 46285*, Richard C. Shelton, M.D., Craig H. Mallinckrodt, Ph.D., Michael J. Robinson, M.D., Madelaine M. Wohlreich, M.D., Joel Raskin, M.D., Michael J. Detke, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that during acute phase treatment with duloxetine, patients within all three cohorts (mild, moderate, and severe baseline symptom severity) exhibited significant improvement in a range of treatment outcomes including the HAMD17 total score and the Maier and retardation subscales.

Summary:

Objective: To determine whether severity of depression affected the efficacy of duloxetine in treating MDD.

Method: Pooled data from 4 double-blind, placebo-controlled studies in which patients with MDD were randomized to duloxetine (60 mg/day) or placebo for 8 or 9 weeks. Patients were retrospectively stratified according to baseline HAMD17 total scores: mild = total score <19 (duloxetine, n=247; placebo, n=184); moderate = 20-24 (duloxetine, n=333; placebo, n=217); severe = 25+ (duloxetine, n=127; placebo, n=87).

Results: Compared with placebo, duloxetine produced significantly greater baseline-to-endpoint mean change in HAMD17 total score, Maier and retardation subscales, HAMD17 Items 1 (depressed mood), 7 (work and activities), and 10 (psychic anxiety) (LOCF analyses; p<.05 for each outcome) in all 3 patient cohorts. For the severely depressed cohort, superiority of duloxetine over placebo was first observed at Week 1 for the Maier and retardation subscales and for HAMD17 individual Items 1 (depressed mood), 2 (guilt), 3 (suicide), and 9 (agitation); Week 2 for HAMD17 total score; and Week 4 for the anxiety/somatization subscale.

Conclusion: As shown here, duloxetine at its recommended therapeutic dose of 60 mg/day demonstrated superior efficacy as compared with placebo in the treatment of MDD, regardless of the baseline severity of depressive symptoms. Funding provided by Eli Lilly and Company

References:

1. Detke MJ, et al. Duloxetine 60 mg once daily dosing versus placebo in the acute treatment of major depression. J Psychiatr Res 2002;36:383-390.
2. Detke MJ, et al. Duloxetine, 60 mg once daily, for major depressive disorder: a randomized double-blind placebo-controlled trial. J Clin Psychiatry 2002;63:308-315.

NR271 Monday, May 22, 3:00 PM - 5:00 PM

Atypical Antipsychotics and the Risk of Menstrual Abnormalities in Bipolar Disorder

Natalie L. Rasgon, M.D. *Stanford University School of Medicine, 401 Quarry Road, Room 2360, Palo Alto, CA, 94305-5723*, Wendy Marsh, M.D., Tasha Glenn, Ph.D., Paul Grof, M.D., Michael Bauer, M.D., Peter C. Whybrow, M.D.

Educational Objectives:

To demonstrate an association between the use of atypical antipsychotics and menstrual abnormalities in women with bipolar disorder.

Summary:

Objective: To investigate whether taking atypical antipsychotics and/or mood stabilizers increased the risk of menstrual abnormalities in women with bipolar disorder.

Method: For 6 months, women prospectively documented mood, menstrual cycle and medications using the ChronoRecord computer software for daily self-reporting. 83 women completed the study returning 14,999 days of data. Medication data from all 411 menstrual cycles was analyzed using a logistic regression.

Results: 50.6% of the women reported menstrual abnormalities. The results of a logistic regression showed an increased risk of menstrual abnormalities associated with antipsychotics alone (odds ratio [OR], 4.65, 95% confidence interval [CI], 2.11-10.3), antipsychotics in combination with carbamazepine (OR 7.4; 95% CI. 2.06-26.7) and antipsychotics in combination with lamotrigine (OR 3.69; 95% CI, 1.37-9.93. Lithium monotherapy was associated with a lower risk of menstrual abnormalities (OR .09, 95% CI, .029-.277). Women with menstrual abnormalities were more likely to report premenstrual worsening of symptoms.

Conclusion: Controlled studies of the impact of specific atypical antipsychotics on menstrual regularity, prolactin levels and ovarian function are indicated for women with bipolar disorder.

References:

1. Rasgon NL, Altshuler LL, Fairbanks L, Elman S, Bitran J, Labarca R, et al. Reproductive function and risk for PCOS in

women treated for bipolar disorder. Bipolar Disord. 2005;7:246-59.

2. Rasgon NL, Reynolds MF, Elman S, Saad M, Frye MA, Bauer M, Altshuler LL. Longitudinal evaluation of reproductive function in women treated for bipolar disorder. J Affect Disord. 2005 Sep 17; [Epub ahead of print].

NR272 Monday, May 22, 3:00 PM - 5:00 PM

Single-Center, Double-Blind, Placebo-Controlled Study of Paroxetine in Dysthymic Disorder

Arun V. Ravindran, M.B. *University of Toronto, Psychiatry, Centre for Addiction and Mental Health, 250 College Street, Toronto, ON, M5T 1R8, Canada*, Colin John Cameron, M.D., Raj Bahtla, M.D., Martha McKay, M.A., Andree Cusi, B.S., Scott Simpson, Ph.D.

Educational Objectives:

1) After a review of the presentation, participants will have a general understanding of the literature on SSRI treatment of Dysthymic Disorder

2) At conclusion of the presentation, participants will have learned the results of this study, specifically, the efficacy and tolerability of paroxetine compared to placebo, as well as the impact on quality of life and coping skills in Dysthymic Disorder

Summary:

Background: Data on the effectiveness of paroxetine in patients with Dysthymic Disorder without comorbid Major Depression is limited.

Method: In a12-week, double-blind, randomized, placebo-controlled study, 45 patients with a diagnosis of Dysthymic Disorder, without Major Depression were recruited. After a single-blind placebo run, patients were randomly assigned to receive paroxetine (N=23) or placebo (N=22). The paroxetine dose was flexible, initiated at 20mg and increased to a maximum dose of 40mg, based on response and tolerability. The efficacy measures included the Hamilton Depression Rating Scale (HAMD), the Clinical Global Impressions - Severity (CGI-S), - Improvement (CGI-I), Cornell Dysthymic Rating Scale (CDRS), and the Beck Depression Inventory (BDI).

Results: Analyses of the mean scores on an intent to treat population were completed for all efficacy measures. The paroxetine group showed a greater reduction than the placebo group in both the CGI-S scores (p=.05) and CGI-I scores (p=.01). Patients treated with paroxetine reported greater improvement in depressive symptoms on the BDI compared to the placebo group (p=.03). Trends were observed in both the HAMD-17 and the CDRS, with a HAMD-17 score reduction of 51% for the paroxetine-treated group, and 34% reduction for the placebo group (p=.08), and a 47% score reduction in the CRDS for the paroxetine group, and 23% for the placebo group (p=.07). A significantly greater proportion of the paroxetine-treated group were identified as responders and remitters relative to placebo group by the final visit. Those treated with paroxetine indicated significantly greater improvement on the Quality of Life Enjoyment and Satisfaction Questionnaire compared with the placebo (p≤ .01). Paroxetine was well tolerated with no serious adverse events reported.

Conclusion: Paroxetine is effective in reducing symptoms and improving quality of life in the short-term treatment of Dysthymic Disorder.

This investigator-initiated study was funded by a grant from Glaxo-Smith Kline.

References:

1. Hellerstein DJ: Dysthymic disorder: integrating research findings into clinical treatment. J Psychiatr Pract. 2001; Sep; 7 (5): 298-309.

2. Ravindran AV, Bialik RJ & Lapierre YD: Therapeutic efficacy of specific serotonin reuptake inhibitors (SSRIs) in dysthymia. Can J Psychiatry 1994; 39: 21-26.

NR273 Monday, May 22, 3:00 PM - 5:00 PM

A Comparative Evaluation of Efficacy Between Alternative Treatments for Acute Mania

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Educational Objectives:

To gain systematic evidence of the relative efficacy of different treatments available for acute mania in bipolar disorder patients.

Summary:

Background: Acute manic episodes in bipolar disorder patients are commonly treated with a variety of drugs. The objective was to comparatively evaluate the clinical efficacy of several antipsychotic therapies along with valproate semisodium and lithium.

Methods: Using Bayesian meta-analysis methods[1,2], we pooled response rates from 11 trials comprising 2421 patients with episodes of acute mania. A hierarchical Bayesian model was used, incorporating random study effects and fixed treatment effects. The response rate was defined as a ≥ 50% improvement in a patient's baseline score assessed using the Young Mania Rating Scale. The 95% Bayesian credible intervals (CIs) were constructed for differences in response rates between each drug.

Results: Compared to the pooled response rate for the placebo groups of 0.2917, the pooled response rates for all therapies were significantly higher: valproate semisodium (0.45), quetiapine (0.45), haloperidol (0.46), aripiprazole (0.48), lithium (0.50), olanzapine (0.54). However, the 95% CIs reported no statistically significant differences in the response rates between these drugs.

Conclusions: There is no statistically significant difference in efficacy between some of the commonly available treatments for acute mania. Physicians should take into account the side-effect profiles of these drugs when treating these patients.

References:

1. Bridle C, Palmer S, et al: A rapid and systematic review and economic evaluation of the clinical and cost-effectiveness of newer drugs for treatment of mania associated with bipolar affective disorder. Health Technology Assessment 2004; 8(19).

2. Hasselbald V. Meta-analysis of multi-treatment studies. Medical Decision Making 1998; 18: 37-43.

NR274 Monday, May 22, 3:00 PM - 5:00 PM

Prevalence and Predictors of Disordered Eating in Bipolar Disorder

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Educational Objectives:

At the conclusion of this session the participant should be cognizant of the high rates of eating disorder co-morbidity in bipolar disorder and its co-occurrence with anxiety disorders.

Summary:

Objective: To determine prevalence and predictors of disordered eating in bipolar disorder.

Methods: 458 patients with bipolar disorder at a specialty clinic (diagnosed by baseline MINI International Neuropsychiatric Interviews) were examined for the presence of co-morbid lifetime eating disorders (LED). LED cases were compared with selected age and gender matched non-LED bipolar controls, and the presence of co-morbid conditions, demographics, and medication use was compared. Prospectively collected assessments of binge purge eating behavior (BPB) were identified using the Clinical Monitoring Form (CMF).

Results: 4% of male and 17% of female patients met criteria for LED. Significant differences were found between patients with and without LED for co-morbid agoraphobia 21% versus 7% ($p<0.01$), Social Phobia 15% versus 5% ($p<0.02$) and PTSD 16% versus 7% ($p<0.05$). Chart review identified 71 BPB cases. LED cases displaying current BPB did not differ from LED cases without BPB for age, bipolar subtype, marital status, educational level, mood stabilizer and atypical antipsychotic use.

Conclusion: Rates of eating disorder are higher in bipolar disorder than the general population. LED bipolar patients are more likely to be female, have co-morbid agoraphobia, social phobia and PTSD than bipolar patients without LED.

References:

1. McElroy S, Kotwal R, Keck P, Askiskal H: Comorbidity of bipolar and eating disorders: distinct or related disorders with shared dysregulations. J Affect Disord 2005; 86: 107-127.
2. Sheehan DV, Lecrubier Y, Sheehan KH, et al.: The Mini-International Neuropsychiartic Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interverview for DSM-IV and ICD-10. J Clin Psychiatry 1998; 59:22-33.

NR275 Monday, May 22, 3:00 PM - 5:00 PM

Comparison of Postpartum and Nonpostpartum Depression on Mothers

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the differences on symptomatology and sociodemographic features between women with postpartum depression and depression on other period of life. Non postpartum women presents more fatigue, uselessness and guilty ideas, depressive mood, suicidal thoughts and history of previous depressive episodes. Not paying attention to these aspects could result in an missdiagnose and insufficient treatment of depression on the differents periods of life.

Summary:

Goal: To compare the depressive symptomatology, the family background and the sociodemographic variations between women with postpartum depression and depression on other period of life.

Metodology: The evaluation was done at three primary medical centers of Santiago, Chile during 2004. 382 women with a major depressive episode, 204 on postpartum period and 178 with a child between 6 and 16 years old. As measuring tools, we used the Edinburgh Postnatal Depression Scale, the Goldberg Health Questionnaire and the MINI. We grouped the results using the SPSS 11.0 and statistical analysis was made by Chi^2 and student tests.

Results: There is a statiscal difference in favour of no postpartum group on depressive mood, fatigue, guilty and uselessness ideas, suicidal thoughts and hystory of previous episodes.

Conclusions: There is evidence that shows the existence of differences on symptomatology and sociodemographic features between these two groups of patients, and according to the litterature, this could be related with the missdiagnose and insufficient treatment of some cases.

Fondecyt project 1040432 and 1040434

References:

1. Whiffen V, Gotlib I: Comparaison of postpartum and nonpostpartum depression: Clinical presentation, psychiatric hystory, and psychosocial functioning. Journal of consulting and clinical psychology 1993; 3: 485-494.
2. Eberhard-Gran M, Tambs K, Opjordsmoen S, Skrondal A, Eskild A: A comparaison of anxiety and depressive symptomatology in postpartum and non-postpartum women. Soc Psychiatry Epidemiol 2003; 38: 551-556.

NR276 Monday, May 22, 3:00 PM - 5:00 PM

The Prevalence of Depressive Symptoms in a Cardiac Rehabilitation Population

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Educational Objectives:

At the conclusion of this poster presentation, the participant should be able to recognize the high prevalence of depressive symptoms in a cardiac rehabilitation population and be aware of their impact on rehabilitation outcomes.

Summary:

Objective: Depressive symptoms, as indicated by a Centre for Epidemiological Studies Depression (CES-D) scale score ≥16, have been associated with poor medical outcomes in cardiac patients. Our purpose was to quantify the prevalence of depressive symptoms in a large cardiac rehabilitation population.

Methods: Depression severity, demographic characteristics, and medication use were assessed in cardiac rehabilitation outpatients at admission, and at 6 and 12 months post-admission. The frequency of depressive symptoms in this population was compared in separate cohorts across the three visits.

Results: 1172 patients were recruited into this study (70.6% male, mean age 61.02 ± 10.98 years). 23.3% of participants displayed at least mild depressive symptoms (CES-D≥16; 27.1% at baseline, 20.3% at 6 months, 16.3% at 12 months), while 10.4% displayed significant depressive symptoms (CES-D≥23; 12.1% at baseline, 9.8% at 6 months, 5.8% at 12 months). Of those with significant depressive symptoms at baseline, 21.7% were receiving antidepressant pharmacotherapy. Significantly fewer patients in each successive cohort had depressive symptoms ($\chi^2=6.225$, $p=0.013$).**Conclusions:** There is a high prevalence of depressive symptoms among cardiac rehabilitation patients, and little pharmacotherapy provided. Further investigation of this sample as it progresses through the program will provide important information regarding the etiology and impact of co-morbid depression on cardiac rehabilitation outcomes.

References:

1. Journal Article - Aben I, Verhey F, Strik J, Lousberg R, Lodder J, Honig A: A comparative study into the one year cumulative incidence of depression after stroke and myocardial infarction. J Neurol Neurosurg Psychiatry 2003; 74:581-585.

2. Journal Article - Frasure-Smith N, Lesperance F, Juneau M, Talajic M, Bourassa MG. Gender, depression, and one-year prognosis after myocardial infarction. Psychosom Med 1999; 61:26-37.

NR277 Monday, May 22, 3:00 PM - 5:00 PM

The Rothschild Scale for Antidepressant Tachyphylaxis (Poop-Out)

Anthony J. Rothschild, M.D. *University of Massachusetts Medical School and the University of Massachusetts Memorial Healthcare, Psychiatry, 361 Plantation Street, Worcester, MA, 01605*

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the signs of antidepressant tachphylaxis (antidepressant "poop-out").

Summary:

Objective: Antidepressant tachyphylaxis (antidepressant "poop-out") is frequently observed in clinical practice. In a 1997 statewide survey in Massachusetts, 92% of psychiatrists had observed this phenomenon in patients who had previously responded to ongoing treatment with SSRIs (Byrne and Rothschild, 1997). Several strategies have been proposed for the treatment of antidepressant tachyphylaxis (Byrne and Rothschild, 1998); however, research has been hampered by the lack of an accepted definition of the phenomena and a reliable and valid assessment tool.

Method: The Rothschild Scale for Antidepressant Tachyphylaxis (RSAT) was developed to better characterize antidepressant tachyphylaxis and consists of 6 self-report items assessing energy level, motivation and interest, cognitive functioning, weight gain, sleep, and sexual functioning. A 7th item, affect, is assessed by the Interviewer. RSAT data will be presented on 50 patients successfully treated for Major Depression who complained of "antidepressant poop-out" but who did not meet criteria for a relapse or recurrence of Major Depression and whose Hamilton Depression Rating Scale Score was < 12, 50 patients with Major Depression who did not complain of "antidepressant poop-out", and 50 normal controls.

Results: RSAT scores for patients complaining of antidepressant "poop-out" (9.7 + 2.9) were significantly higher (p<.05) than patients who did not complain of "poop-out" (4.5 + 2.8) or normal controls (3.8 + 1.2). Using a cut-off of an RSAT score > 7, the RSAT had 94% sensitivity and 92% specificity for detecting patients who complained of antidepressant "poop-out".

Conclusions: The RSAT is a reliable and valid instrument for assessing antidepressant tachyphylaxis ("poop-out").

References:

1. Byrne S, Rothschild AJ: Psychiatrists' responses to failure of maintenance therapy with antidepressants. Psychiatric Services, 1997; 48:835-837.
2. Bryne SE, Rothschild AJ: Loss of antidepressant efficacy during maintenance therapy: possible mechanisms and treatments. J Clin Psychiatry, 1998; 59:279-288.

NR278 Monday, May 22, 3:00 PM - 5:00 PM

Effect of High or Low Levels of Agitation on the Antimanic Response to Aripiprazole

Gary S. Sachs, M.D. *Harvard-Massachusetts General Hospital, 50 Staniford Street, Suite 580, Boston, MA, 02114*, David Crandall, Ph.D., Linda Rollin, Ph.D., Andy Forbes, Ph.D., Rolando Gutierrez-Esteinou, M.D., Andrei Pikalov, M.D., Raymond Sanchez, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to appreciate that acute manic/mixed episodes of bipolar I disorder are comprised of a spectrum of symptoms, including various levels of agitation. They should be aware that aripiprazole is an effective treatment for patients with bipolar I disorder, regardless of their level of agitation, as demonstrated by a pooled analysis of efficacy data from two 3-week placebo-controlled trials.

Summary:

Objective: Assess the influence of agitation on the effectiveness of aripiprazole in patients experiencing acute manic/mixed episodes of bipolar I disorder.

Methods: Patients from two 3-week, double-blind, placebo-controlled trials were randomized to aripiprazole 30 mg/d (n = 259) or placebo (n = 253). High agitation was assessed as a PANSS Excited Component (PEC) score of ≥14 and a ≥4 score on at least one PEC item (excitement, hostility, tension, uncooperative, poor impulse control). Baseline-to-endpoint differences were measured within high and low agitation groups using: Young Mania Rating Scale (YMRS) total score, Clinical Global Impression-Bipolar Disorder (CGI-BP), and PEC item scores. Mean change from baseline comparisons were analyzed using ANCOVA model, controlling for treatment, protocol, and baseline value.

Results: Aripiprazole was associated with significant improvement in YMRS and CGI-BP scores from baseline to study endpoint compared with placebo in both high and low agitation groups. The mean difference in YMRS total scores between aripiprazole and placebo was -6.7 for the high agitation group and -4.2 for the low agitation group ($P < 0.05$). The mean difference in CGI-BP total scores between aripiprazole and placebo was -0.8 for the high agitation group and -0.6 for the low agitation group ($P < 0.05$). Highly agitated patients treated with aripiprazole also showed significantly improved PEC scores compared with placebo (mean difference = -2.6, $P < 0.05$.). For patients with low agitation, aripiprazole improved endpoint PEC scores at a trend level compared with placebo (mean difference = -1.3; $P = 0.07$).

Conclusions: Aripiprazole is effective at reducing symptoms of manic/mixed episodes in patients with bipolar I disorder, regardless of baseline level of agitation.

References:

1. Keck PE Jr, Marcus R, Tourkodimitris S, et al, Aripiprazole Study Group: A placebo-controlled, double-blind study of the efficacy and safety of aripiprazole in patients with acute bipolar mania. Am J Psychiatry 2003; 160:1651-1658.
2. Vieta E, Bourin M, Sanchez R, et al; on behalf of the Aripiprazole Study Group:.

NR279 Monday, May 22, 3:00 PM - 5:00 PM

A Canadian Naturalistic Study of a Community-Based Cohort Treated for Bipolar Disorder

Doron Sagman, M.D. *Lilly Research Laboratories, Eli Lilly Canada, 3650 Danforth Avenue, Toronto, ON, M1N 2E8, Canada*, Bobbie Lee, M.S.C., Ranjith Chandrasena, M.D., Trevor Boudreau, B.S.C., Elizabeth Brunner, M.D.

Educational Objectives:

At the conclusion of this session, the participant should recognize clinical and health outcomes in a community sample of bipolar patients treated naturalistically over a one year period with olanzapine and/or other medications.

Summary:

Introduction: With limited duration and rigorous criteria, randomized clinical trials may not fully reflect the actual population who ultimately receive medication in usual clinical care settings. CNS-

Bipolar was a one-year, prospective, observational study of community-based adult outpatients with bipolar disorder.

Methodology: 496 patients experiencing an exacerbation of manic symptoms in the course of usual care were enrolled. Clinical and health outcomes were observed at 1, 6 and 12 months. The primary objective of this study was to measure change in mania symptoms from baseline to 1 month as measured by the Young Mania Rating Scale (YMRS) in two groups: The Olanzapine Group (n=287) consisted of patients whose medication adjustment was either an increase in the dose or addition of olanzapine. The Other Group (n=209) consisted of patients requiring an increase in dose or addition of a medication other than olanzapine. YMRS and MADRS were used to measure symptomatic change, response (YMRS ≤8, MADRS ≤14 at 1 month) and relapse (YMRS or MADRS >14 after initial response). Resource utilization and substance abuse were also observed.

Results: 391 (78.8%) patients completed the study; 223 (77.7%) in the Olanzapine Group and 168 (80.4%) in the Other Group. On average, both groups demonstrated an improvement on YMRS score at one month: 10.8 (Olanzapine) and 9.5 (Other); response rates were 44% (Olanzapine) and 34% (Other). Relapse rates at 12 months were 6% (Olanzapine) and 20% (Other). Resource utilization throughout the study did not generally differ between the two groups; about 16% of all patients had at least one hospitalization and about 10% had at least one emergency room visit. About 10% reported substance abuse.

Conclusions: All treatments demonstrated clinically meaningful symptomatic improvement with over ¾ of patients completing the one year naturalistic study.

References:

1. Sanger TM, Grundy SL, Gibson PJ, et al: Long-term olanzapine therapy in the treatment of bipolar I disorder: an open-label continuation phase study. J Clin Psychiatry 2001; 62:273-281.
2. Yatham L, Kennedy SH, O'Donovan C, et al: CANMAT Guidelines for the management of patients with bipolar disorder: consensus and controversies. Bipolar Disorders 2005; 7:Supplement 3.

NR280 Monday, May 22, 3:00 PM - 5:00 PM

Off-Label Use of Levetiracetam in Patients With Cyclothymia

Marco Sarchiapone *University of Molise, Department of Health Sciences, Via De Sanctis, Campobasso, 86100, Italy*, Giovanni Camardese, M.D., Vladimir Carli, M.D., Chiara Cuomo, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant will be aware of clinical data about using Levetiracetam as a mood stabilizer il cyclothymia.

Summary:

Objective: Levetiracetam is well-tolerated anticonvulsant with a unique mechanism of action and positive effects in an animal model of mania. Preliminary data suggest a potential mood stabilizer activity of levetiracetam in bipolar patients. The aim of our research is to evaluate the use of levetiracetam in patients with cyclothymia.

Methods: 28 patients suffering from cyclothymic disorder, according to DSM-IV-TR criteria, have been recruited, in a 12 week open-label trial, at Gemelli Hospital in Rome. Patients with comorbidity for other psychiatric disorders have been excluded, except for cluster B personality disorder. After evaluation with Hamilton Depression Rating Scale (HDRS), Hamilton Anxiety Rating Scale (HARS) and a Visual Analogue Scales (VAS) on depressed mood, levetiracetam was administered in fixed doses (500 mg b.i.d). Psychiatric assessments have been repeated after 2, 4, 6, 8 and 12 weeks.

Results: 7 patients (25%) dropped-out. Levetiracetam has been well tolerated with only 2 discontinuations due to adverse events. In 15 (71,4%) of 21 patients who completed the trial a reduction >50% has been observed at VAS. In 10 patients a significant reduction of anxiety on HARS has been reported.

Conclusions: Our results support preliminary findings on potential mood stabilizing efficacy of levetiracetam so cyclothymic patients may respond to levetiracetam therapy. Our study was limited by the open-label design and lack of a placebo group.

References:

1. Lamberty Y, Margineanu DG, Klitgaard H. Effect of the New Antiepileptic Drug Levetiracetam in an Animal Model of Mania. Epilepsy Behav. 2001 Oct;2(5):454-459.
2. Post RM, Altshuler LL, Frye MA et al. Preliminary observations on the effectiveness of levetiracetam in the open adjunctive treatment of refractory bipolar disorder. J Clin Psychiatry. 2005 Mar;66(3):370-4.

NR281 Monday, May 22, 3:00 PM - 5:00 PM

Tolerability and Effectiveness of Lamotrigine With and Without Concomitant Valproate in Patients With Bipolar I Disorder

Elias Sarkis *Sarkis Family Psychiatry, 529 NW 60th Street, Gainesville, FL, 32607-2008*, Jay Graham, Jeremy Roberts, Robert Leadbetter, Kevin Nanry

Educational Objectives:

At the conclusion of this presentation, the participant should be able understand patient response and tolerability to lamotrigine treatment.

Summary:

Objective: Lamotrigine was effective and well tolerated in clinical trials of bipolar disorder.[1] The current analysis investigated whether the clinical response and adverse-event profiles differs in patients treated with lamotrigine (alone or with other medications) with or without concomitant valproate.

Methods: A "post hoc" analysis was conducted from a prospective, open-label study of lamotrigine [2] in patients with bipolar I disorder designed to assess the rate of rash in patients with or without specific dermatological precautions. Lamotrigine was administered for 12 weeks, including a 5-week titration period (target dosage 200 mg/day). Clinical Global Impression-Bipolar version (CGI-BP) Severity scores were recorded at baseline, week-5, and week-12 visits, and adverse events were recorded at weeks 5 and 12.

Results: Of the 1175 patients included in the study, 260 (22%) were receiving concomitant valproate. Statistically significant improvement was observed with lamotrigine with and without valproate from baseline in mean ± SD CGI-BP Severity Overall scores at week 5 (-0.6 ± 1.18 with valproate and -0.8 ± 1.04 without valproate, $P < 0.0001$ for both groups) and at week 12 (-0.8 ± 1.40 with valproate and -0.8 ± 1.04 without valproate, $P < 0.0001$ for both groups). Patients without valproate had significantly greater mean CGI-BP Improvement scores at week 12 than those receiving valproate ($P = 0.0025$). At least one adverse event was reported by 63% of patients with valproate and 58% of those without valproate. No serious rash was reported in the study.

Conclusion: These findings suggest that lamotrigine is well tolerated in patients with bipolar I disorder with and without concomitant valproate.

This study was supported by GlaxoSmithKline.

References:

1. Bowden CL. Lamotrigine in the treatment of bipolar disorder. Expert Opin Pharmacother. 2002;3:1513-1519.
2. Ketter TA et al. The Effect of Dermatologic Precautions on the Incidence of Rash with Addition of Lamotrigine in the Treatment of Bipolar I Disorder. J Clin Psych. In Press.

NR282 Monday, May 22, 3:00 PM - 5:00 PM

Socioeconomic Status in Bipolar Disorder Versus the General Population

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the socioeconomic disadvantages of bipolar disorder.

Summary:

Objective: To study socio-economic status in bipolar patients compared to the general population.

Method: 91 patients with DSM-IV bipolar disorder consecutively admitted to a psychiatric acute in-patient unit (Bipolar Research And Innovation Network-Norway, BRAIN) were compared with 54 039 individuals from the general population (Nord-Troendelag Health Study, HUNT). Data from patients recruited through the BRAIN study from other areas of Norway is currently being included in the study.

Results: The educational level was significantly higher in the bipolar group than in the general population with no gender difference. In the bipolar group 52 % of the men and 76 % of the women were out of work, compared to 13 % of the men and 30 % of the women in the general population. 40 % of the bipolar women had disability pension compared to 13 % in the control group. In the general population lived 75 % of the men and 80 % of the women with av partner compared with only 37 % of the men and 53 % of the women in the bipolar group.

Conclusion: Acutely admitted bipolar patients have a higher educational level, but experience a lower socio-economic status compared to the general population in Norway.

References:

1. Tsuchiya KJ, Agerbo E, Byrne M, Mortensen PB: Higher socioeconomic status of parents may increase risk for bipolar disorder in the offspring. Psychol Med 2004; 34:787-93.
2. Abood Z, Sharkey A, Webb M, Kelly A, Gill M: Are patients with bipolar affective disorder socially disadvantaged? A comparison with a control group. Bipolar Disord 2002; 4:243-248.

NR283 Monday, May 22, 3:00 PM - 5:00 PM

Randomized, Double-Blind, Pilot Trial Comparing Lamotrigine Versus Citalopram for the Treatment of Bipolar Depression

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Educational Objectives:

At the conculsion of this presentation, the participant will be more aware of the efficacy of treatments for bipolar depression

Summary:

Introduction: Uncertainty exists regarding the best approach for treating bipolar depression among patients already receiving a first-line mood stabilizer. The aim of this study was to compare adding a second mood stabilizer or an antidepressant at this treatment decision point.

Methods: Twelve-week, randomized, double-blind pilot trial comparing the addition of lamotrigine or citalopram for bipolar depressed patients on mood stabilizer medication. Change in depressive symptoms and risk of switch were examined.

Results: Twenty subjects were randomized. Each treatment group experienced a significant mean reduction in total MADRS scores (citalopram Δ -14.2, $p = 0.002$; lamotrigine Δ -13.3, $p = 0.001$), and there was no significant difference between treatment groups ($p = 0.78$). Total response rates increased from 31.6% at week 6 to 52.6% at week 12. One out of ten patients in each group experienced a switch to hypomania.

Discussion: Results of this small trial suggest that both lamotrigine and citalopram appear to be reasonable choices as add-on acute treatment for bipolar depression, with response rates continuing to rise considerably past 6 weeks of treatment.

References:

1. Young LT, Joffe RT, Robb J, et al. Double-Blind Comparison of Addition of a Second Mood Stabilizer Versus an Antidepressant to an Initial Mood Stabilizer for Treatment of Patients with Bipolar Depression. Am J Psychiatry 2000;157:124-126.
2. Calabrese J, Bowden C, Sachs G, et al. A double-blind placebo-controlled study of lamotrigine monotherapy in outpatients with bipolar I depression. Lamictal 602 Study Group. J Clin Psychiatry 1999;60:79-88.

NR284 Monday, May 22, 3:00 PM - 5:00 PM

Randomized, Double-Blind, Placebo-Controlled Study of Desvenlafaxine Succinate in MDD

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to:

1.Understand the efficacy of desvenlafaxine succinate (DVS) in treatment of major depressive disorder in adult outpatients.

2. Understand the safety of DVS in treatment of major depressive disorder in adult outpatients.

Summary:

Objectives: Evaluate the antidepressant efficacy and safety of desvenlafaxine succinate (DVS) in adults with MDD.

Methods: In a phase 3, multicenter, randomized, double blind, placebo-controlled, parallel-group study, adult outpatients aged 18 to 75 years with a primary diagnosis of MDD were treated with fixed doses of DVS 200 or 400 mg daily for 8 weeks. The primary efficacy measure was change from baseline on the 17-item Hamilton Rating Scale for Depression ($HAM\text{-}D_{17}$); the key secondary efficacy measure was the Clinical Global Impression-Improvement (CGI-I) Scale. Other secondary efficacy measures included response and remission, improvement on the visual analog scale-pain intensity (VAS-PI), and other symptomatic and functional outcomes. Safety was evaluated via assessment of adverse events (AEs), discontinuation due to AEs, physical examination, 12-lead electrocardiogram, vital signs, laboratory determinations, and the discontinuation-emergent signs and symptoms (DESS) checklist.

Results: A total of 375 subjects were randomized to treatment; 373 were included in the safety analyses and 369 in the intent-to-treat efficacy analyses. At final on-therapy evaluation, adjusted mean change from baseline in HAM-D_{17} total score was greater for DVS 200 mg (-12.6, *P*=.002) and DVS 400 mg (-12.1, *P*=.008) versus placebo (-9.3); mean CGI-I scores were lower for DVS 200 mg (2.2, *P*=.004) and DVS 400 mg (2.3, *P*=.028) versus placebo (2.7). Both doses were significantly better than placebo on MADRS scores, CGI-Severity, and HAM-D_{17} response. DVS 200 mg was also significantly better than placebo on remission, VAS-PI overall scores and some component scores. DVS 400 mg was significantly better than placebo on some VAS-PI component scores. Most AEs were mild or moderate in severity, and safety assessments revealed few clinically significant changes.

Conclusions: These data provide support for the efficacy and safety of DVS for treatment of MDD.

References:

1. Zajecka JM, Albano D: SNRIs in the management of acute major depressive disorder. J Clin Psychiatry 2004; 65(Suppl 17):11-18.
2. Muth EA, Moyer JA, Haskins JT, Andree TH, Husbands GEM: Biochemical, neurophysiological, and behavioral effects of WY-45,233, its enantiomers, and other identified metabolites of the antidepressant venlafaxine. Drug Dev Res 1991; 23:191-199.

NR285 Monday, May 22, 3:00 PM - 5:00 PM

Inpatient Treatment of Mood Disorders: Diagnostic Issues, Treatment Strategies, and Outcome

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Educational Objectives:

To learn about the clinical characteristics and treatment approaches of patients presenting and being admitted for refractory mood disorders.

Summary:

Objective: To describe demographic features, clinical characteristics, and treatment strategies of patients admitted to a specialized inpatient unit for mood disorders. *Method:* The sample consisted of patients who were admitted between December 2003 and June 2005. The differences between admission and discharge Beck Depression Inventory-II, Beck Anxiety Inventory, and the Quality of Life in Depression Scale scores were analyzed. In addition, variables such as age, gender, medications, preadmission versus discharge diagnoses, and history of suicide attempts were examined. *Results:* Overall, fifty-three cases, twenty-six males and twenty-seven females, yielded useable data out of an available total of seventy-four cases (73%). Preadmission diagnoses included major depression (36.5%), bipolar II (25%), bipolar I (17.3), bipolar unspecified (7.7%), and other (13.5%). The average number of medications at admission was four with 52.8% of patients being treated with antidepressants and 67.9% of patients being treated with mood stabilizers. Upon discharge, the diagnoses were bipolar II (47.2%), bipolar I (18.9%), major depression (18.9%), bipolar NOS (9.4%), and schizoaffective disorder (5.7%). The average number of medications at discharge was three with 13.2% of patients being treated with antidepressants and 84.9% being treated with mood stabilizers. The difference between the number of medications taken at admission versus discharge was significant ($p<.01$), as were the differences between pre and post-treatment measures of symptom severity ($p<.001$). The decrease in antidepressant use and the increase in the use of mood stabilizers from admission to discharge were also significant ($p<.01$). *Limitations:* This was a naturalistic study, and the data was collected in a non-blind fashion. *Conclusions:* The findings suggest that in an inpatient mental health care setting, the treatment of mood disorders, and specifically bipolar disorder is effective. The results also lend support to our previously reported findings among outpatients that misdiagnosis of bipolar disorders as resistant depression is a common occurrence.

References:

1. Sharma V; Khan M; and Smith A: A closer look at treatment resistant depression: is it due to a bipolar diathesis? Journal of Affective Disorders 2005; 84: 251-527.
2. Semenova O; Ivanov V; Tochilov V; and Isacsson G: Demography, clinical characteristics and current treatment of in-patients with bipolar disorder in a Russian psychiatric hospital. Int J of Psychiatry in Clin Practice 2004; 8: 161-168.

NR286 Monday, May 22, 3:00 PM - 5:00 PM

Efficacy of Ziprasidone in Dysphoric Mania: Pooled Analysis of Two Double-Blind Studies

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to demonstrate the effectiveness of ziprasidone monotherapy in treating patients with dysphoric mania, a common and often difficult to treat subtype of acute bipolar mania.

Summary:

Objective: To assess the efficacy of ziprasidone in the treatment of depressive symptoms associated with dysphoric mania, a common and often difficult to treat subset of acute bipolar mania. Dysphoric mania is defined as mania accompanied by clinically significant depressive symptoms.[1]

Methods: Pooled data were examined from 2 similarly designed, 3-week placebo-controlled trials in acute bipolar mania. [2] Patients were considered to have dysphoric mania if they scored >2 on at least 2 items of the extracted HAM-D. Changes in HAM-D scores from baseline to days 2,4,7,14 and 21 were evaluated by a mixed model analysis of variance. Additional assessments included changes in the MRS (Mania Rating Scale), CGI, PANSS, and GAF scores.

Results: Starting on day 4, HAM-D scores were significantly lower at all visits in patients treated with ziprasidone compared to those treated with placebo ($P< .05$). Ziprasidone- treated patients also demonstrated significant improvements on the MRS, CGI, PANSS, and GAF scores compared to placebo.

Conclusions: In placebo-controlled trials, ziprasidone significantly improved depressive and other symptoms associated with dysphoric mania.

Support for this study was provided by Pfizer.

References:

1. McElroy SL, Keck PE Jr, Pope HG Jr, et al. Clinical and research implications of the diagnosis of dysphoric or mixed mania or hypomania. Am J Psychiatry 1992: 149: 1633-1644.
2. Keck PE Jr, Versiani M, Potkin S, et al, for the Ziprasidone in Mania Study Group. Ziprasidone in the treatment of acute bipolar mania: a three-week, placebo-controlled, double-blind, randomized rial. Am J Psychiatry 2003; 160: 741-748.

NR287 Monday, May 22, 3:00 PM - 5:00 PM

Increased Mood Episode Cycling With Antidepressants in Bipolar Disorder: A Randomized Clinical Trial

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Educational Objectives:

At the end of this presentation, participants should be able to understand the effects of long-term antidepressant use on the overall number of mood episodes in bipolar patients.

Summary:

Objective: Previous studies conflict about long-term antidepressant treatment of bipolar depression. Some double-blind placebo controlled data suggest that tricyclic antidepressants may worsen the course of rapid-cycling bipolar disorder (1), while other observational data in non-rapid cycling bipolar patients suggest that antidepressant discontinuation leads to more depressive relapse (2). This is the first randomized study of antidepressant discontinuation in long-term treatment of bipolar disorder with modern antidepressants.

Method: In interim analysis of 5-year study (n=66), subjects recovered from a depressive episode on mood stabilizer plus antidepressant were openly randomized to continue (LT; n=30) or discontinue (ST; n=36) antidepressants. Subject mood was noted at each visit with measures of affective morbidity. Data are presented as adjusted in regression models for rapid cycling, gender, age, substance abuse, psychosis, and antidepressant attitude.

Results: ST group had fewer depressed episodes (β=-0.55, 95% CI[-1.48, 0.39]). ST group had a slight, though statistically insignificant, benefit over LT group for number of manic episodes observed (β=-0.082; 95% CI[-0.42, 0.25]).

Conclusions: These data are consistent with superiority of antidepressant discontinuation, compared with antidepressant continuation, in terms of mood episodes observed. Antidepressant continuation was associated with increased mood episode cycling rates, even in a mostly non-rapid cycling population.

Funding Source: NIMH grant MH-64189-05 (Dr. Ghaemi)

References:

1. Wehr TA, Goodwin FK: Can antidepressants cause mania and worsen the course of affective illness? Am J Psychiatry 1987; 144(11):1403-1411.
2. Altshuler LL, et al: Impact of antidepressant discontinuation after acute bipolar depression remission on rates of depressive relapse at 1-yr follow-up. Am J Psychiatry 2003; Jul;160(7):1252-62.

NR288 Monday, May 22, 3:00 PM - 5:00 PM

Metabolic Effects of Divalproex Sodium Extended-Release in Acute Mania

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Educational Objectives:

Examine the metabolic effects of divalproex extended-release (ER) in a three-week trial of bipolar I disorder, manic or mixed type.

Summary:

Objective: Examine the metabolic effects of divalproex extended-release (ER) in a three-week trial of bipolar I disorder, manic or mixed type.

Methods: A 21-day, randomized, placebo-controlled, parallel-group study was conducted in adult patients with bipolar I disorder. Divalproex Extended Release dosing was initiated at 25 mg/kg/day QD, and adjusted to a target serum valproate level of 85-125 mcg/mL. Metabolic assessments (e.g. weight, glucose, and cholesterol) were included as standard safety measures during the study. Post-hoc analyses examined the metabolic changes associated with divalproex Extended Release in the total study population, and in various sub-populations.

Results: Analyses included 377 subjects (192 divalproex Extended Release ; 185 placebo). Divalproex Extended Release produced significant reductions in total cholesterol, LDL and HDL cholesterol compared to placebo in the total study population, with no significant change in HDL/LDL ratio. Treatment with divalproex Extended Release was associated with significant weight gain compared to placebo ($p < 0.05$), but was not associated with any significant changes in glucose.

Conclusion: Although divalproex Extended Release is associated with weight gain, it is not associated with other negative metabolic changes such as increased glucose and cholesterol.

References:

1. Bowden CL, Singh V: Valproate in bipolar disorder: 2000 onwards. Acta Psychiatr Scand Suppl 2005; 426:13-20.
2. Stoner SC, Dubisar BM, Lea JW, Marken PA, Ramlatchman LV, Reynolds JB: Extended-release divalproex sodium for mood stabilization. Pharmacotherapy 2004; 24:1147-1153.

NR289 Monday, May 22, 3:00 PM - 5:00 PM

Why the First Two Weeks of Treatment With Antidepressants Really Matter: Results From the Mirtazapine Database

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that clinically relevant treatment decisions with antidepressants can be made as early as after 2 weeks of treatment.

Summary:

Background:

Clinicians currently assume that most antidepressants have a delayed onset of efficacy. Therefore the clinical changes during the first 2 weeks of treatment are usually not regarded as important for the assessment of treatment outcome. However, the delayed onset hypothesis has been questioned by recent data.

Methods:

We analyzed the time course of improvement and response of individual patients from various RCTs with different antidepressants as well as the utility of early improvement during individual treatment course as a predictor of later treatment outcome in a large data set (n>7300). Improvement was defined as a HAM-D-17/ MADRS score reduction of > 20% compared with baseline. Stable response (> 50% score reduction from baseline on HAMD-17 or MADRS) or remission (reduction to <7 points on HAMD-17 or <12 points on MADRS) was defined as being present both at week 4 and week 6.

Results:

Our results yielded clear evidence that the improvement occurred in a majority of all responders/remitters within the first two weeks of treatment and that it predicts later stable response with high sensitivity (mirtazapine: 90%; SSRI: 87.7%; TCA: 82.9%) . Moreover, in a first prospective trial early improvement showed excellent sensitivity as a predictor of stable response or remission within 6 weeks of treatment comparing mirtazapine (sensitivity for remission: 100%) with venlafaxine (sensitivity for remission: 94.1%) in major depression.

Conclusions:

These empirically derived data suggest that the early individual course of improvement is of major relevance for a patient's individual treatment outcome and provide important clinical clues for an individually tailored antidepressant treatment. The results indicate that if a patient has not shown an improvement after 2 weeks, there is little chance that she/he will still become a responder or remitter with unchanged treatment within 6 weeks.

Funding Source: This research was supported by Organon International Inc.

References:

1. Szegedi A, Muller MJ, Anghelescu I, Klawe C, Kohnen R, Benkert O: Early improvement under mirtazapine and paroxetine predicts later stable response and remission with high sensitivity in patients with major depression. J Clin Psychiatry 2003; 64(4):4.
2. Posternak MA, Zimmerman M: Is there a delay in the antidepressant effect? A meta-analysis. J Clin Psychiatry 2005; 66(2):148-58.

NR290 Monday, May 22, 3:00 PM - 5:00 PM

Baseline Characteristics and Outcomes in First- and Multiple-Episode Patients With Acute Mania

Mauricio F. Tohen, M.D. *Eli Lilly and Company, One Lilly Corporate Center, Indianapolis, IN, 46285,* Iris Goetz, M.D., Eduard Vieta, M.D., Ana Maria Gonzalez-Pinto, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should understand differences in clinical characteristics and time to recovery between patients with bipolar disorder presenting with a first episode or multiple episodes during the course of treatment for acute mania.

Summary:

Objectives: To describe the baseline characteristics and recovery of patients with first-episode or multiple episodes who enrolled in EMBLEM (European Mania in Bipolar Longitudinal Evaluation of Medication study).

Methods: EMBLEM is a 2-year prospective, observational study conducted in 14 European countries to evaluate outcomes in patients experiencing a manic or mixed episode.

Results: Out of 3566 patients, 7% enrolled with a first episode, and 75% with multiple episodes. First-episode patients were significantly younger than those with multiple episodes (38.3 versus 44.6yrs, p<.0001), had significantly lower BMI (22.49 versus 26.26, p<.0001), and a greater percentage reported current (22% versus 11%, p<.0001) or past (19% versus 13%, p=.01) cannabis use. First-episode patients had significantly higher baseline YMRS total (28.6 versus 26.3, p=.0006), and CGI-mania (5.0 versus 4.8, p=.001) scores, and lower CGI-depression (1.7 versus 1.9, p=.004) and HAMD-5 total (2.5 versus 2.8, p=.05) scores, relative to multiple episode patients. Time to recovery was significantly shorter for first-episode patients relative to those with multiple episodes (37.7 versus 43.7 days, p=.0115).

Conclusions: With 3566 patients EMBLEM represents one of the largest naturalistic studies of outcomes in bipolar disorder. First-episode patients presented with different illness characteristics at baseline and achieved recovery more rapidly relative to those with multiple episodes.

The EMBLEM study is supported by Eli Lilly & Company.

References:

1. HARO JM et al.: European mania in bipolar longitudinal evaluation of medication (EMBLEM) study: study design and recruitment of a 2-year, pan-European, observational health outcomes study in bipolar disorder. Bipolar Disorders 2003:5 (Suppl.1); P82.
2. GOETZ I et al.: Functional impairment in patients with acute mania: Baseline results of the Emblem study. Bipolar Disorder.(in press).

NR291 Monday, May 22, 3:00 PM - 5:00 PM

Olanzapine in the Treatment of Acute Mania in Adolescents with Bipolar I Disorder: A Three-Week, Randomized, Double-Blind Placebo-Controlled Study

Mauricio F. Tohen, M.D. *Eli Lilly and Company, One Lilly Corporate Center, Indianapolis, IN, 46285,* Ludmila Kryzhanovskaya, M.D., Gabrielle A. Carlson, M.D., Melissa P. DelBello, M.D., Robert A. Kowatch, M.D., Joe Biederman, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to evaluate the efficacy and safety of olanzapine in the treatment of bipolar mania in adolescents.

Summary:

Objective: To evaluate the efficacy and safety of olanzapine for the treatment of acute mania in adolescents with bipolar disorder.

Methods: Patients 13-17 years of age with a manic or mixed bipolar episode received either olanzapine (2.5-20 mg/day; N=107) or placebo (N=54) in a 3-week, multicenter, randomized, double-blind, parallel trial. The primary efficacy variable was mean change from baseline to endpoint in Young Mania Rating Scale (YMRS) total score

Results: Significantly greater baseline-to-endpoint reductions in YMRS total score were observed for olanzapine-treated relative to placebo-treated patients (-17.7 versus -10.0, p<.001; Effect Size, 0.84). A greater proportion of olanzapine-treated patients met response and remission criteria (44.8% versus 18.5%; p=.002 and 35.2% versus 11.1%; p=.001, respectively) and reached those criteria significantly more rapidly (p=.003 and p=.002, respectively) relative to those who received placebo. The incidence of treatment-emergent weight gain ≥7% (41.9% versus 1.9%; p<.001), and hyperprolactinemia were significantly greater for olanzapine-treated relative to placebo-treated patients. The incidence of treatment-emergent abnormal levels of glucose, cholesterol, triglycerides or uric acid did not differ significantly between treatment groups.

Conclusions: Olanzapine was effective in the treatment of adolescents with bipolar mania. The types of adverse events appeared to be similar to those in adults, but may have differed in magnitude.

This study was funded and conducted by Eli Lilly and Company

References:

1. Frazier JA, Biederman J, Tohen M, Feldman PD, Jacobs TG, Toma V, Rater MA, Tarazi RA, Kim GS, Garfield SB, Sohma M, Gonzalez-Heydrich J, Risser RC, Nowlin ZM: A prospective open-label treatment trial of olanzapine monotherapy in children and adolesce.
2. Tohen, M., Jacobs, T. G., Grundy, S. L., Banov, M. C., McElroy, S. L., Janicak, P. G., Zhang, F., Toma, V., Francis, B. J.,

Sanger, T. M., Tollefson, G. D., and Breier, A. Efficacy of olanzapine in acute bipolar mania: a double-blind, placebo-control.

NR292 Monday, May 22, 3:00 PM - 5:00 PM

Longitudinal Neta-Analysis of the Surrogate Suicide Items of the Hamilton and/or the Montgomery-Asberg Rating Scales Comparing Mirtazapine Versus Placebo

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that treatment with the antidepressant mirtazapine is beneficial for depressed patients with suicidal thoughts.

Summary:

Objective: Antidepressants are under close scrutiny by regulatory authorities in many countries, especially with regard to the risk of these agents causing suicidal thoughts or behaviors. The objective of this analysis was to examine the effects of mirtazapine versus placebo on suicide risk, derived from the HAMD or MADRS suicide item scores as a surrogate.

Methods: All acute, randomized, double-blind, placebo-controlled mirtazapine trials in MDD were pooled. Suicidal risk was defined as a suicide item score on the HAMD and/or the MADRS being ≥ 3. Treatment effects (adjusted for baseline suicidal risk and/or severity) of mirtazapine as compared to placebo, sensitivity of the analyses to drop-outs, and predictive value to actual suicide-related events (as classified by the Columbia University group) were assessed.

Results: Overall there were 1,147 mirtazapine-treated patients and 707 patients treated with placebo with a baseline score of ≥ 3 on the suicide item parameter. During the first week of treatment, mirtazapine treated patients showed a trend toward a lower incidence of suicide risk versus those treated with placebo (as measured by the respective HAMD/MADRS items). From Week 2 onwards, mirtazapine treated patients had a statistically significantly lower incidence of suicidal risk (items HAMD/MADRS). To the contrary, placebo-treated patients were at increased suicidal risk (as measured by the respective HAMD/MADRS items); odds ratios at week 1, 2, 3, 4 and 6 were, 1.54 (P=0.16), 4.1 (P<0.001), 3.6 (P=0.005), 4.2 (P=0.01) and 3.7 (P=0.01), respectively. Subgroup results in the vast majority of patients that were not at suicidal risk at baseline were very similar.

Conclusion: This analysis reveals evidence that suicide risk, as measured by suicide item scores from either HAMD or MADRS, is reduced with active mirtazapine treatment compared to those taking placebo.

Funding Source: This research was supported by Organon International Inc.

References:

1. Arif Khan et al.: Suicide rates in clinical trial of SSRIs, other antidepressants, and placebo: Analysis of FDA reports. Am J Psychiatry 2003; 160: 790-792.

2. Goran Isacsson and Charles L. Rich: Antidepressant drug use and suicide prevention. Int Rev Psychiatry 2005; 17(3):153-162 .

NR293 Monday, May 22, 3:00 PM - 5:00 PM

Minimal Abuse Potential of Bupropion, a Norepinephrine-Dopamine Reuptake Inhibitor

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Educational Objectives:

At the conclusion of this presentation, the participant should have a better understanding of the brain pathways and neurotransmitters involved in drug abuse. Additionally, at the conclusion of this presentation, the participant should have a better understanding of the neurophysiologic mechanisms that underlie the differences in abuse potential between bupropion and psychostimulants.

Summary:

Objective: Bupropion blocks the neuronal reuptake of norepinephrine and dopamine. It is structurally similar to amphetamine and other central stimulants, although unlike these drugs, neither bupropion nor its metabolites cause presynaptic release of monoamines, and the rate and extent of dopamine transporter blockade differs significantly between bupropion and other centrally acting psychostimulants. A concern for drugs that block dopamine reuptake is the potential for abuse. This review examines the literature regarding the abuse potential of bupropion, and discusses potential reasons that bupropion is unlike centrally acting psychostimulants in its abuse potential.

Methods: A Medline search was conducted for articles published on the abuse potential of bupropion through February, 2005. The key word bupropion was combined with the other key words abuse, dependence, tolerance, and withdrawal. Articles were included if they presented animal or human data relating to the abuse potential of bupropion.

Results: The possibility that bupropion has amphetamine-like abuse potential has been suggested by findings of psychostimulant properties in animal studies. Human studies have not, however, shown bupropion to have significant reinforcing properties. Moreover, there has been no evidence of abuse clinically.

Conclusions: Pharmacologically, although bupropion does increase dopamine levels through dopamine reuptake blockade, it is distinct from cocaine and amphetamine in that it does not cause presynaptic release of catecholamine neurotransmitters. Both the extent and time course of dopamine transporter (DAT) occupancy by bupropion and its active metabolites distinguish it from psychostimulants. Bupropion has been shown to have a 25% DAT occupancy, with binding at the DAT sustained over 24-hours following steady-state dosing with the sustained-release formulation of bupropion. These important differences between bupropion and centrally active psychostimulants appear to be sufficient to prevent bupropion from having reinforcing properties and instead, to demonstrate a very low potential for abuse.

References:

1. Volkow ND, Fowler JS, Wang GJ, Goldstein RZ: Role of dopamine, the frontal cortex and memory circuits in drug addition: Insight form imaging studies. Neurobio Learning and Memory 2002;78:610-624.

2. Fibiger HC: Mesolimbic dopamine: an analysis of its role in motivated behavior. Semin Neurosci 1993;5:321-327.

NR294 Monday, May 22, 3:00 PM - 5:00 PM

Presentation and Validation of a New Scale for Assessment of Depression in Spanish-Speaking Population

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702, Lima 18, Lima, Lima 18, Peru, Santiago M. Stucchi-Portocarrero, M.D., Nancy Valdez-Huarcaya, Psy.D., Miriam Cabra-Bravo, R.N., María I. Zapata-Vega, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to demonstrate understanding of the psychometric properties of a newly developed depression scale for Spanish-speaking populations and to recognize the need for culture-informed assessment instruments.

Summary:

Objective: Presentation and validation of a 20-item new depression scale (NDS) based on the Major Depressive Episode Criterion-A (DSM-IV) and specifiers for melancholic and atypical features in a Spanish-speaking Peruvian sample.

Method: 226 non-psychotic outpatients seen for their first diagnostic interview were included. The patients completed three assessment instruments: the NDS, the Zung Self-Rating Depression Scale (ZSDS) and the Major Depression Module of the SCID. All patients were interviewed by a psychiatrist who documented all major Axis I disorders. If depression was present, its severity was documented using clinical criteria and the corresponding item of the BPRS.

The internal consistency, and convergent, content, and discriminant validity of the NDS were studied.

Results: The NDS internal consistency analysis showed a Cronbach's alpha of 0.86. High convergence between total scores of the NDS and the ZSDS (r=0.79) was found. Comparison of diagnoses of depression made by the NDS and the SCID showed an area under the ROC curve (auROC) of 0.87; the sensitivity (Sn) was 81.32% and the specificity (Sp) was 80% for a cut-off score of 26.5. Comparison of the NDS with the psychiatrist's diagnosis showed an auROC of 0.83; the Sn was 77.67% and the Sp was 72.32% for a cut-off score of 25.5. Similar values were found for diagnoses made by the ZSDS in comparison with the SCID and the psychiatrist. The NDS mean scores showed significant statistical differences between groups of subjects classified (by the SCID and the psychiatrist) as having a major depressive episode and other disorders. The severity of depression according to the NDS significantly correlated to the psychiatrist rating, the BPRS and ZSDS.

Conclusions: The NDS achieved similar psychometric values as compared with other widely used and well established instruments. Its use may be promissory for screening, clinical care and research purposes in Spanish-speaking population.

References:

1. Handbook of psychiatric measures. Edited by Rush Jr AJ, Pincus HA, First MB, Blacker D, Endicott J, Keith SJ, Phillips KA, Ryan ND, Smith Jr GR, Tsuang MT, Widiger TA, Zarin DA. Washington, DC, American Psychiatric Association, 2000.
2. Aragones Benaiges E, Masdeu Montala RM, Cando Guasch G, Coll Borras G: [Diagnostic validity of Zung's self-rating depression scale on primary care patients]. Actas Esp Psiquiatr 2001; 29(5):310-6.

NR295 Monday, May 22, 3:00 PM - 5:00 PM

Relationship Functioning in Bipolar Disorder

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to:

(i) observe the relationship and sexual functioning in a large Canadian sample of BD subjects

(ii) note factors related to sexual adjustment in bipolar disorder

Summary:

Introduction: Bipolar Disorder (BD) may affect adjustment in relationships, including sexual functioning. This study assesses whether gender, relationship status, or bipolar subtype affects the sexual/spousal functioning in BD.

Method: 188 BD subjects (females = 107) were categorized by marital status and rated on frequency of dating and marital friction. Sexual satisfaction and level of sexual activity were measured using a modified version of the Social Adjustment Scale (Bauer, 2001). Mood symptoms were rated using the Longitudinal Interval Follow-Up Evaluation (LIFE).

Results: Marital status was not associated with gender or bipolar subtype; nor was marital friction. For those eligible to date, 60% were not dating, and 26% were frequently dating. 60% of the total sample were not sexually active recently. For those sexually active, 43% reported sexual satisfaction as fair or poor. Using logistic regression, both gender and relationship status were predictive of sexual satisfaction. Males and those who were married/cohabiting reported more satisfaction with sexual relationships. Current mood symptoms were not related to marital status, gender or sexual satisfaction.

Conclusion: Relationship functioning in BD is affected by gender and marital status. Findings will be discussed in the context of the study limitations as well as other literature.

References:

1. Bauer MS. Kirk GF. Gavin C. Williford WO. Determinants of functional outcome and healthcare costs in bipolar disorder: a high-intensity follow-up study. Journal of Affective Disorders 2001; 65(3):231-41.
2. Litzinger S. Gordon KC. Exploring relationships among communication, sexual satisfaction, and marital satisfaction. Journal of Sex & Marital Therapy 2005; 31(5):409-24.

NR296 Monday, May 22, 3:00 PM - 5:00 PM

Validated Tools Available in Spanish for Bipolar Disorder Screening

Jose Sanchez-Moreno *SPAIN*, Eduard Vieta, Guadalupe Sanchez, Silvia Zaragoza-Domingo, Juan Lahuerta, Manuel De Gracia

Educational Objectives:

At the conclusion of this poster participants will have available specific tools to screen for bipolar disorder among spanish-speaking psychiatric patients.

Summary:

Objective: Bipolar Disorder (BD) is underdiagnosed resulting in inadequate patient management. This may improve by using available validated screening tools. Those developed in English-speaking countries need validation for use in Spanish-speaking subjects. The Mood Disorder Questionnaire (MDQ) is a widely used, self-applied questionnaire. Hypomania Checklist-32 (HCL-32) is a self-applied questionnaire being developed in European countries.

Method: Spanish versions of the questionnaires (MDQ and HCL-32) were validated in a study conducted in 236 subjects recruited at 15 Psychiatric centres in Spain, belonging to 4 diagnostic groups: BDI, BDII, depressive disorder and healthy controls.

Results: MDQ exhibits a high degree of internal consistency with a sensitivity of 0.6 and specificity of 0.98 for BD detection with 7 positive symptoms, clustering and, moderate or worse problems deemed postive. Its psychometric properties are similar to those

of the English version. HCL-32 exhibited high internal consistency with a higher sensitivity (0.85) but lower specificity (0.79) with 14 positive answers. MDQ and HCL-32 questionnaires are displayed and their respective properties compared.

Conclusions: MDQ can be employed in Spanish-speaking populations for BD screening. HCL-32 may also provide adequate BD screening. Adaptation of the vocabulary is indicated for the use of these questionnaires in Spanish-speaking subpopulations outside Spain.

References:

1. Hirschfeld RM, Holzer C, Calabrese JR, Weissman M, Reed M, Davies M, Frye MA, Keck P, McElroy S, Lewis L, Tierce J, Wagner KD, Hazard E: Validity of the mood disorder questionnaire: a general population study. Am J Psychiatry 2003; 160(1):178-18.
2. Angst J, Adolfsson R, Benazzi F, Gamma A, Hantouche E, Meyer TD, Skeppar P, Vieta E, Scott J: The HCL-32: towards a self-assessment tool for hypomanic symptoms in outpatients. J Affect Disord 2005; 88(2):217-233.

NR297 Monday, May 22, 3:00 PM - 5:00 PM

Placebo Response in Studies of Bipolar Mania

B. Timothy Walsh, M.D. *Columbia University & The New York State Psychiatric Institute, Department of Psychiatry, 1051 Riverside Drive, Unit #98, New York, NY, 10032-2603*, Robyn Sysko, M.S.

Educational Objectives:

At the conclusion of this presentation, the participant should understand the rate of placebo response in studies of bipolar mania to a non-specific intervention.

At the conclusion of this presentation, practitioners will be able to recognize the similarities and differences in the rates of placebo response in studies of major depression and bipolar mania.

Summary:

Objective: A previous review (Walsh, Seidman, Sysko, & Gould, 2002) found that response to placebo in studies of major depression was variable, substantial, and increasing over time. The purpose of this study was to examine placebo response rates in trials of patients with acute bipolar mania.

Method: Similar to the procedures of the Walsh et al. (2002) study, we searched MEDLINE for all placebo-controlled trials published between January 1980 and November 2005 in which patients with bipolar mania were randomly assigned to receive medication or placebo. To date, the review has identified 14 studies of bipolar mania meeting our criteria. Ten studies published between 1999 and 2005 used a response criterion of a 50% or greater decrease on the Young Mania Rating Scale (YMRS).

Results: At the baseline assessment, the average YMRS score was 29.78, and over the course of treatment, YMRS scores among patients receiving placebo decreased an average of 7.29 points. The average placebo response rate on the YMRS was 31.1% (range of 17%-44%). There was no indication of an association between the year of publication and placebo response rate (r= 0.017, p= 0.961).

Conclusions: The overall response rate to placebo (31.1%) in studies of bipolar mania was similar to the rate observed in major depression (29.7%). Over a limited number of years, there was no indication of a change in placebo response in studies of bipolar mania. In an attempt to compare response rates from older to more recently published papers, we will present data from a larger number of papers and will assess changes over time in the effect size of placebo. These additional analyses will permit a discussion of similarities and differences in response to placebo between studies of major depression and acute mania, including whether placebo response in bipolar mania is changing over time.

References:

1. Walsh BT, Seidman SN, Sysko R, Gould M: The placebo response in studies of major.
2. Keck PE Jr, Mendlwicz J, Calabrese JR, Fawcett J, Suppes T, Vestergaard PA, Carbonell C. A review of randomized, controlled clinical trials in acute mania. J Affect Disord 2000; 59 Suppl 1: S31-S37.

NR298 Monday, May 22, 3:00 PM - 5:00 PM

Efficacy of Quetiapine Monotherapy in Bipolar I Depression: Combined Results From Two Double-Blind, Placebo-Controlled Studies

Richard H. Weisler, M.D. *Duke University Medical Center, University of North Carolina at Chapel Hill, Department of Psychiatry and Behavioral Science, 700 Spring Forrest Road, Suite 125, Durham, NC, 27609*, Robert Arvekvist, Göran Stening, Wayne Macfadden, M.D.

Educational Objectives:

At the conclusion of this session, the participants will be able to: 1) evaluate efficacy and tolerability data for quetiapine in depressive episodes in bipolar I disorder; and 2) use this information in clinical practice for the management of depressive episodes in these patients.

Summary:

Objective: To determine the efficacy and tolerability of quetiapine monotherapy for the treatment of depressive episodes in bipolar I disorder.[1,2]

Methods: This was an evaluation of 694 patients with bipolar I disorder pooled from 2 double-blind, randomized, placebo-controlled 8-week studies of quetiapine (300 or 600 mg/d; once-daily, evening dosing) that included patients with bipolar I or II depression (DSM-IV). MADRS and HAM-D scores were assessed weekly throughout the study. The primary endpoint was change in MADRS total score from baseline at Week 8 (analyzed using mixed-effect model, repeated-measures).

Results: Improvements in mean MADRS total score from baseline (range 30.1-30.7 for the 3 groups) were significantly greater with quetiapine 300 and 600 mg/d than with placebo from the first assessment (Week 1) through to Week 8. The changes from baseline at Week 8 with quetiapine 300 and 600 mg/d were -19.40 and -19.60, respectively; both were $P<0.001$ versus placebo (change from baseline -12.56). The MADRS effect sizes were 0.78 and 0.80 for quetiapine 300 and 600 mg/d, respectively. Improvements from baseline in mean HAM-D scores at Week 8 were also significantly greater with quetiapine 300 and 600 mg/d than with placebo (-15.29 and -15.63; both $P<0.001$ versus -10.04) The HAM-D effect sizes were 0.82 and 0.87, respectively. Overall, there were significant improvements in the primary and secondary outcomes with both 300 and 600 mg/d quetiapine, without major differences in the doses. Common adverse events included dry mouth (300 mg/d: 40.9%; 600 mg/d: 44.0%; placebo: 12.2%), somnolence (32.8%, 31.0%, 7.0%), and sedation (25.9%, 26.7%, 8.3%). Adverse events were generally mild in intensity in the 2 studies.

Conclusion: Quetiapine monotherapy is significantly more effective than placebo for the treatment of depressive episodes in bipolar I disorder and is well tolerated.

Supported by funding from AstraZeneca Pharmaceuticals LP.

References:

1. Keck PE, Jr., Nelson EB, McElroy SL. Advances in the pharmacologic treatment of bipolar depression. Biol Psychiatry 2003;53(8):671-9.

2. Calabrese JR, Keck PE, Jr., Macfadden W, Minkwitz M, Ketter TA, Weisler RH, et al. A randomized, double-blind, placebo-controlled trial of quetiapine in the treatment of bipolar I or II depression. Am J Psychiatry 2005;162(7):1351-60.

NR299 Monday, May 22, 3:00 PM - 5:00 PM

The Safety of Combination Therapy With Carbamazepine Extended-Release Capsules for Bipolar I Disorder

Richard H. Weisler, M.D. *UNC/Duke University, 700 Spring Forrest Road, Suite 125, Durham, NC, 27609*, Thomas Gazda, M.D., David A. Sack, M.D., Robert Riesenberg, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant will have a better understanding of the safety of carbamazepine in combination with atypical antipsychotic medications.

Summary:

Objective: To evaluate the safety of carbamazepine extended-release capsules (CBZ-ERC) "(Equetro™; Shire; Wayne, Pa)" in combination with other psychotropic medications for the treatment of Bipolar I Disorder.

Methods: An 8-week open-label observational study was conducted at 11 sites. Fifty-three subjects were enrolled (mean age 38.8, 64% female); patients were at least 18 years old, most recent episode manic or mixed. The primary objective was to evaluate the safety of CBZ-ERC in combination with other psychotropic medications for the treatment of Bipolar I Disorder.

Results: Thirty-five of 53 patients (66%) completed the study. Reasons for early termination included lost to follow-up (7 patients), adverse events (9 patients), and withdrawn consent (2 patients). All patients took concomitant psychotropic medications, including aripiprazole (28%), olanzapine (11%), quetiapine (51%), and risperidone (13%). Adverse events were those common to anticonvulsants and included somnolence, dizziness, nausea, and vomiting. There were 3 instances of serious adverse events, including abdominal pain, worsening of bipolar symptoms (screen failure), and priapism.

Conclusions: Carbamazepine extended-release capsules in combination with other psychotropic medications were found to be generally safe in combination with other psychotropic medications. These data are encouraging, but need to be considered in the context of the small scale of this study.

References:

1. 1. Weisler RH, Keck PE Jr, Swann AC, Cutler AJ, Ketter TA, Kalali AH. Extended-release carbamazepine capsules as monotherapy for acute mania in bipolar disorder: a multicenter, randomized, double-blind, placebo-controlled trial. J Clin Psychiatry. 20.
2. 2. Okuma T, Yamashita I, Takahashi R, et al. Comparison of the antimanic efficacy of carbamazepine and lithium carbonate by double-blind controlled study. Pharmacopsychiatry. 1990;23:143-150.

NR300 Monday, May 22, 3:00 PM - 5:00 PM

Locus-of-Control and Outcome of Treatment for MDD

Stephen B. Woolley, M.P.H. *Institute of Living, 200 Retreat Avenue, Hartford, CT, 06106*, Shoshana Pavel, B.A., John W. Goethe, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to:

(1) discuss locus of control

(2) describe the potential role in treatment outcomes of patients with MDD.

Summary:

Objective: To investigate the association between internal locus-of-control (LOCI) and severity of MDD and the effect of LOCI on the outcome of treatment for MDD.

Methods: Patients (n=138) were interviewed in-person and their medical charts abstracted. Information obtained included personal, psychosocial, historical mental health and treatment, and MDD symptoms. A subset (n=50) was re-interviewed three months later. Associations between LOCI scores[1] (continuous and categories-low, moderate, high) and outcomes (including the Beck Depression Inventory 13-item scale; BDI) at baseline and follow-up were measured by calculating correlation coefficient, *t*-test, and chi-square statistics.

Results: Mean BDI score at baseline was 21.7 (range 0-37;n=138), and declined 44% during follow-up ($p<.001$;n=49). High LOCI scores were (a) directly associated with baseline ($p=.097$) and follow-up BDI scores ($p=.087$) and with patients changing the way they deal with stress ($p=.016$), (b) inversely associated with dissatisfaction with life ($p=.012$) and with difficulty with family/friends ($p=.038$), and (c) not associated with change in BDI ($p=.483$), having severe symptoms ($p=.403$), adherence to prescriptions ($p=.667$), or readmission ($p=.423$). Life events scale[2] scores were associated with LOCI ($p=.091$), but did not modify the association between LOCI and follow-up BDI scores ($p=.554$).**Conclusions:** LOCI was not associated with changes in depression during and after treatment but was associated with level of depression. Patients' LOCI did not explain improvement/non-improvement among MDD inpatients. Life event scale scores were associated with LOCI, but did not explain the association between LOCI and BDI scores.

References:

1. Valecha GK, Ostrom TM. An abbreviated measure of internal-external locus of control. J Pers Assess 1974;38:369-376.
2. Cochrane R, Robertson A. The life events inventory: a measure of the relative severity of psycho-social stressors. J Psychosom Res 1973;17:135-140.

NR301 Monday, May 22, 3:00 PM - 5:00 PM

Efficacy and Tolerability Effects of L-Methionine, Betaine, and Folate on Anxiety and Overall Psychiatric Symptoms in Unipolar Depression

Benjamin Zablotsky, B.A. *Cambridge Health Alliance, 1493 Cambridge Street, Cambridge, MA, 02139*, Robert T. Dunn, M.D., Vanessa A. Stan, A.B.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand the short-term effects of L-methionine, betaine and folate in the treatment of anxiety and overall psychiatric symptoms in unipolar depression.

Summary:

Objective: Prior studies suggest that S-adenosylmethionine (SAMe) is effective in the treatment of unipolar depression (1), and that methionine and betaine can increase SAMe in brain (2). This first prospective study examined the efficacy of the combination of L-methionine, betaine and folic acid in the treatment of anxiety and overall psychiatric symptoms in unipolar depression.

Method: An open label, prospective, non-randomized, 6-week study of fixed doses of methionine, betaine and folate, was conducted in depressed unipolar outpatients. No psychotropic medications were allowed. The Zung Anxiety scale (ZA), Young Mania Rating Scale (YMRS), and Brief Psychiatric Rating Scale (BPRS)

were administered at every visit to detect anxiety, manic and psychotic symptoms, respectively.

Results: Scores were obtained in 5 patients (3M, 2F). Mean ZA scores did not change from baseline (34.8±6.3) to endpoint (28.8±5.1), where (t=1.66, p=0.13). Mean YMRS scores did not change from baseline (1.2±1.0) to endpoint (1.0±1.0), where (t= 0.32, p=0.76). There was a trend for BPRS scores to improve from baseline (31.6±6.3) to endpoint (25.2±2.3), where (t=2.13, p=0.07).

Conclusion: The combination of L-methionine, betaine and folate does not cause or worsen anxiety, manic or psychotic symptoms in acute unipolar depression. Full data will be presented.

Funding Source: NARSAD

References:

1. Alpert JE, et al.: S-adenosyl-L-methionine as an adjunct for resistant major depressive disorder: an open trial following partial or nonresponse to selective serotonin reuptake inhibitors or venlafaxine. J Clin Psychopharmacol 2004; Dec:24(6):661-664.

2. Baldessarini RJ: Alterations in tissue levels of tissue levels of S-adensylmethionine. Biochem Pharmacol 1966; 15:741-748.

NR302 Monday, May 22, 3:00 PM - 5:00 PM

Diagnosing MDD: A Psychometric Evaluation of the *DSM-IV* Symptom Criteria

Mark Zimmerman, M.D. *Rhode Island Hospital, Psychiatry, 235 Plain Street, Suite 501, Providence, RI, 02905*, Joseph B. McGlinchey, Ph.D., Diane D. Young, Ph.D., Iwona Chelminski, Ph.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to describe the psychometric performance of the DSM-IV diagnostic criteria for major depressive disorder.

Summary:

Background: The diagnostic criteria for depression were developed on the basis of clinical experience rather than empirical study. Although they have been available and widely used for many years, few studies have examined the psychometric properties of the DSM criteria for major depression. In the present report from the Rhode Island Methods to Improve Diagnostic Assessment and Services (MIDAS) project we examined whether criteria such as insomnia, fatigue and impaired concentration that are also diagnostic criteria for other disorders are less specific than the other DSM-IV depression symptom criteria. We also conducted a regression analysis to determine whether all criteria are independently associated with the diagnosis of MDD. **Method:** One thousand five hundred and thirty-eight psychiatric outpatients were administered a semi-structured diagnostic interview. We inquired about all of the symptoms of depression for all patients. **Results:** All of the DSM-IV symptom criteria for MDD were significantly associated with the diagnosis. Contrary to our prediction, symptoms such as insomnia, fatigue, and impaired concentration, which are also criteria of other disorders, generally performed as well as the criteria that are unique to depression such as suicidality, worthlessness, and guilt. The results of the regression analysis, which controlled for symptom covariation, indicated that five symptoms (increased weight, decreased weight, psychomotor retardation, indecisiveness, and suicidal thoughts) were not independently associated with the diagnosis of depression. **Conclusion:** While all diagnostic criteria for MDD are more frequent in depressed than nondepressed patients, they are not all independently associated with diagnosis. It may therefore be possible to reduce the number of diagnostic criteria for depression without reducing diagnostic validity.

References:

1. Breslau N, Davis, G (1985) Refining DSM-III criteria in major depression. An assessment of the descriptive validity of criterion symptoms. Journal of Affective Disorders. 9:199-206.

2. Buchwald A, Rudick-Davis, D (1993) The symptoms of major depression. Journal of Abnormal Psychology. 102:197-205.

NR303 Monday, May 22, 3:00 PM - 5:00 PM

Diagnosing MDD: Is There Justification for Compound Symptom Criteria?

Mark Zimmerman, M.D. *Rhode Island Hospital, Psychiatry, 235 Plain Street, Suite 501, Providence, RI, 02905*, Joseph B. McGlinchey, Ph.D., Diane D. Young, Ph.D., Iwona Chelminski, Ph.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to describe the three ways the DSM-IV diagnostic criteria for major depressive disorder are constructed, and indicate whether there is empirical support for combining multiple symptoms into single criteria.

Summary:

Background: The DSM-IV symptom inclusion criteria for the diagnosis of MDD are constructed in three ways_single symptom criteria, compound criteria encompassing opposite variants of the same disturbance, and compound criteria encompassing related problems. In the present report from the Rhode Island Methods to Improve Diagnostic Assessment and Services (MIDAS) project we tested the following 3 hypotheses: 1) the components of Compound-Opposite criteria rarely occur simultaneously; 2) the components of the Compound-Related criteria frequently occur simultaneously; and 3) the components of the Compound-Related criteria more frequently co-occur than other pairs of the MDD criteria. We also examined how many patients would be rediagnosed if the compound criteria were split into separate items. **Method:** One thousand eight hundred psychiatric outpatients were evaluated with a semistructured diagnostic interview. We inquired about all of the DSM-IV diagnostic criteria for MDD for all patients. **Results:** As hypothesized, the symptoms of the Compound-Opposite criteria usually did not co-occur, whereas the symptoms of the Compound-Related criteria frequently were present simultaneously. However, the results also indicated that other pairs of symptoms were as likely to co-occur, and were as strongly associated, as the symptoms of the Compound-Related criteria. When the compound criteria were subdivided, and the diagnostic threshold for MDD was kept constant, only a small percentage of patients were reclassified from a noncase to a case. **Conclusion:** The findings provide mixed support for the inferred assumptions hypothesized to underlie the composition of the DSM-IV criteria for MDD. Combining multiple symptoms into single criteria has minimal impact on diagnosis.

References:

1. Breslau N, Davis, G (1985) Refining DSM-III criteria in major depression. An assessment of the descriptive validity of criterion symptoms. Journal of Affective Disorders. 9:199-206.

2. Buchwald A, Rudick-Davis, D (1993) The symptoms of major depression. Journal of Abnormal Psychology. 102:197-205.

NR304 Monday, May 22, 3:00 PM - 5:00 PM

Diagnosing MDD: Can Some Symptoms Be Eliminated From the Diagnostic Criteria?

Mark Zimmerman, M.D. *Rhode Island Hospital, Psychiatry, 235 Plain Street, Suite 501, Providence, RI, 02905*, Joseph B. McGlinchey, Ph.D., Diane D. Young, Ph.D., Iwona Chelminski, Ph.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to describe a new approach towards determining whether, for disorders diagnosed based on a minimum number of features from a list, any criteria can be eliminated because they do not contribute to diagnostic determinations.

Summary:

Background: All criteria used to diagnose a psychiatric disorder should contribute to distinguishing cases from noncases. The principal of parsimony argues for defining a disorder with as few criteria as possible. Thus, criteria that do not contribute to the case-noncase distinction should be eliminated because they unnecessarily increase the complexity of the definition of the disorder. In polythetically defined disorders such as MDD, diagnosis is based on the presence of a minimum number of features from a list. For a criterion to be retained on such a list it should contribute to distinguishing between individuals with and without MDD. Simply demonstrating that a criterion is significantly more common in individuals with MDD than individuals without MDD is not a demonstration of its necessity. To demonstrate an impact on diagnosis, it should be shown that eliminating the criterion from the list results in individuals being reclassified from being a case to a noncase. A criterion does not contribute to determining caseness if its elimination does not result in diagnostic reclassification. The goal of this report from the Rhode Island Hospital Methods to Improve Diagnostic Assessment and Services (MIDAS) project was to determine if any of the criteria of MDD are candidates for elimination because of their lack of impact on diagnosis. **Method:** One thousand eight hundred psychiatric outpatients were evaluated with a semistructured diagnostic interview. We inquired about all of the DSM-IV diagnostic criteria for MDD for all patients. **Results:** The results indicated that the symptoms of increased weight, decreased weight and indecisiveness rarely influenced diagnostic classification, and thus are candidates for elimination. **Conclusion:** Some of the symptoms used to diagnose MDD do not contribute to distinguishing depressed cases from noncases and thus can be eliminated without compromising the validity of the diagnostic criteria.

References:

1. Breslau N, Davis, G (1985) Refining DSM-III criteria in major depression. An assessment of the descriptive validity of criterion symptoms. Journal of Affective Disorders. 9:199-206.
2. Buchwald A, Rudick-Davis, D (1993) The symptoms of major depression. Journal of Abnormal Psychology. 102:197-205.

NR305 Monday, May 22, 3:00 PM - 5:00 PM

Diagnosing MDD: Relationship Between Number of Symptoms and the Diagnosis of Disorder

Mark Zimmerman, M.D. *Rhode Island Hospital, Psychiatry, 235 Plain Street, Suite 501, Providence, RI, 02905*, Joseph B. McGlinchey, Ph.D., Diane D. Young, Ph.D., Iwona Chelminski, Ph.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to describe how the requirement of low mood or anhedonia for the diagnosis of major depression does not have a significant impact on diagnostic determination.

Summary:

Background: The symptom inclusion criteria for DSM-IV MDD consist of a list of nine characteristic features of depression, at least five of which must be present. Two of the criteria for MDD, low mood and anhedonia, are accorded greater importance than the remaining seven criteria in that one of these two features is required for the diagnosis. The implicit assumption underlying this organization of the criteria is that some individuals might meet five of the nine criteria without experiencing low mood or anhedonia and thus be inappropriately diagnosed with major depression. We are not aware of any studies that have examined this assumption. In the present report from the MIDAS project we examined how many psychiatric outpatients meet five of the nine criteria for MDD without simultaneously experiencing either low mood or anhedonia. If this pattern is rare or does not exist, then the method of counting criteria to diagnose major depression could be simplified to a straightforward five out of nine. **Method:** One thousand eight hundred psychiatric outpatients were evaluated with a semistructured diagnostic interview. We inquired about all of the DSM-IV diagnostic criteria for MDD for all patients. **Results:** Twenty-seven (1.5%) patients reported five or more criteria in the absence of low mood or anhedonia. More than half (n=16) of these 27 patients were diagnosed with MDD or bipolar disorder, depressed type, in partial remission, bipolar disorder mixed type (n=1), or bipolar disorder not otherwise specified (n=1). Six of the remaining 11 patients were diagnosed with depressive disorder not otherwise specified. Thus, few patients who met five or more of the MDD criteria were not diagnosed with a depressive disorder. **Conclusion:** The diagnostic criteria for MDD can be simplified to a straight-forward symptom count without reference to the necessity of low mood or anhedonia.

References:

1. Background: The symptom inclusion criteria for DSM-IV major depressive disorder (MDD) consist of a list of nine characteristic features of depression, at least five of which must be present. Two of the criteria for MDD, low mood and anhedonia, are ac.
2. Buchwald A, Rudick-Davis, D (1993) The symptoms of major depression. Journal of Abnormal Psychology. 102:197-205.

NR306 Monday, May 22, 3:00 PM - 5:00 PM

Diagnosing MDD: Applying the *DSM-IV* Exclusion Criteria in Clinical Practice

Mark Zimmerman, M.D. *Rhode Island Hospital, Psychiatry, 235 Plain Street, Suite 501, Providence, RI, 02905*, Joseph B. McGlinchey, Ph.D., Diane D. Young, Ph.D., Iwona Chelminski, Ph.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to describe the impact of the DSM-IV exclusion criteria on the diagnosis of major depressive disorder.

Summary:

Background: To be diagnosed with DSM-IV MDD, a patient must meet five out of nine symptom criteria, one of which is depressed mood or pervasive loss of interest or pleasure. Once a patient has reached this symptom threshold, there are several "exclusionary criteria" that need to be passed in order to receive the diagnosis. The symptoms must cause significant distress or impairment in functioning, the symptoms cannot be caused by substance use or a general medical condition, and the symptoms cannot be better accounted for by bereavement. Finally, the presence of psychotic symptoms not coincident with the depressive symptoms excludes the diagnosis. We are not aware of any studies of psychiatric patients that have examined the impact of all of these exclusionary rules on the diagnosis of MDD in clinical prac-

tice. It is important for clinicians to know how often each of these factors might exclude the diagnosis of MDD so that they can be more or less vigilant to their presence. The goal of the present report from the Rhode Island Methods to Improve Diagnostic Assessment and Services (MIDAS) project was to examine the impact of the DSM-IV exclusion rules on the diagnosis of MDD. **Method:** 1,800 psychiatric outpatients were evaluated with a semi-structured diagnostic interview. We inquired about all of the DSM-IV diagnostic criteria for MDD for all patients, and for patients meeting the symptom inclusion criteria we evaluated the presence of each of the exclusion criteria. **Results:** In total, 38 (3.0%) of the 947 patients meeting the DSM-IV symptom inclusion criteria were excluded from a diagnosis of MDD or bipolar depression. **Conclusion:** These results suggest that the DSM-IV exclusion criteria for MDD had only a modest impact on diagnosis in psychiatric outpatients. The potential influence of different settings on diagnostic exclusion will be discussed.

References:

1. Spitzer RL, Wakefield, JC (1999) DSM-IV diagnostic criterion for clinical significance: Does it help solve the false positives problem? Am J Psychiatry. 156:1856-1864.
2. Zimmerman M, Spitzer, R (2005) Psychiatric Classification. In Kaplan and Sadock's Comprehensive Textbood of Psychiatry (ed. B.Sadock, V. Sadock), pp. 1003-1034. Philadelphia: Lippincott, Williams, & Wilkins.

NR307 Monday, May 22, 3:00 PM - 5:00 PM

Diagnosing MDD: Performance of an Objective Test as a Diagnostic Criterion

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Educational Objectives:

At the conclusion of this presentation the participant should be able to describe the difference between evaluating a test as a diagnostic tool versus a diagnostic criterion.

Summary:

Background: Considerable research has evaluated biological and psychological tests for various psychiatric disorders; however, few objective tests are included in DSM-IV as diagnostic criteria. It was recently suggested that existing tests are insufficiently accurate to be included in the DSM. While it is true that there are limitations in the sensitivity and/or specificity of such tests, this should not rule them out as effective diagnostic criteria. Studies examining the diagnostic efficiency of the DSM criteria sets demonstrate that the individual criteria vary in their sensitivity and specificity. In the present report we suggest changing the perspective used to evaluate the performance of biological and psychological measures from the traditional one examining them as diagnostic tests to one in which these measures are evaluated as diagnostic criteria. To our knowledge no previous investigators have compared the psychometric performance of an objective test to the psychometric performance of the DSM-IV symptom criteria. The recent report from the committee to develop a research agenda for the initial planning phase for DSM-V discussed the use of self-report symptom scales as possible diagnostic criteria. In the present report from the Rhode Island Methods to Improve Diagnostic Assessment and Services (MIDAS) project we examined the performance of a self-report depression questionnaire as a diagnostic criterion for MDD. **Methods:** We compared the performance of the Diagnostic Inventory for Depression (DID) to the performance of the MDD symptom criteria in 1,138 psychiatric outpatients. **Results:** The diagnostic efficiency of the DID was similar to the anhedonia criterion, and superior to all of the remaining DSM-IV MDD symptom criteria except low mood. **Discussion:** A standardized self-report depression questionnaire could function quite well as a diagnostic criterion. We discuss conceptual issues related to the possible inclusion in DSM-V of a self-administered depression symptom scale as a diagnostic criterion.

References:

1. Kupfer D, First, M, Regier, D (2002) A Research Agenda For DSM-V. Washington: American Psychiatric Association.
2. Rounsaville B, Alarcon, R, Andrews, G, Jackson, J, Kendell, R, Kendler, K (2002) Basic nomenclature issues for DSM-V. In A Research Agenda for DSM-V (eds D. Kupfer, M. First, & D. Regier), pp. 1-29. Washington: American Psychiatric Association.

NR308 Monday, May 22, 3:00 PM - 5:00 PM

Diagnosing MDD: Family History as a Diagnostic Criterion

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Educational Objectives:

At the conclusion of this presentation the participant should be able to describe issues that are unique to the use of trait markers such as genetic and family history variables as diagnostic criteria.

Summary:

Background: Since depression runs in families a question arises as to whether family history information should be considered when diagnosing depression. The text of DSM-IV indicates that a family history of mood disorder should sometimes be considered when trying to distinguish between MDD and other conditions such as catatonic schizophrenia. The question posed herein is how well family history of depression performs as a diagnostic criterion, and how does it perform compared to the DSM-IV symptom criteria. **Methods:** 1,800 psychiatric outpatients were evaluated with a semistructured diagnostic interview as part of a research assessment infrastructure that has been embedded in the Rhode Island Hospital Department of Psychiatry outpatient practice. Family history diagnoses were based on the Family History Research Diagnostic Criteria (FH-RDC). We constructed a continuum of family history morbidity based on the number of first-degree family members with a history of depression and whether the family member was treated for their depression. **Results:** Family history information was collected on 9,763 first-degree relatives of 1,776 patients. The sensitivity of the family history criterion was lower than each of the symptoms. Based on the broadest definition of the family history variable the specificity was also lower than all other symptoms. Based on the narrowest definition (two or more family members who were treated for depression), the specificity was higher than all of the symptom criteria though sensitivity dropped to 15%. **Conclusion:** Overall as a diagnostic criterion, a family history of depression did not perform as well as the DSM-IV symptom criteria. Consistent with the familial nature of depression, the family history variable performed better as a diagnostic criterion when considering diagnosis from a lifetime, rather than a current, perspective. This has implications for the future consideration of genetic markers as diagnostic criteria.

References:

1. Charney D, Barlow, D, Botteron, K, Cohen, J, Goldman, D, Gur, R, Lin, K, Lopez, J, Meador-Woodruff, J, Moldin, S, Nestler, E, Watson, S, Zalcman, S (2002) Neuroscience research agenda to guide development of a pathophysiologically based classificatio.

2. Weissman M, Wickramaratne, P, Nomura, Y, Warner, V, Verdeli, H, Pilowsky, D, Grillon, C, Bruder, G (2005) Families at high and low risk for depression: A 3-generation study. Arch Gen Psychiatry. 62:29-36.

NR309 Monday, May 22, 3:00 PM - 5:00 PM

Diagnosing MDD: Are Patients Who Deny Low Mood a Distinct Subgroup?

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Educational Objectives:

At the conclusion of this presentation the participant should be able to describe the validity of diagnosing depression in patients who do not report clinically significant depressed mood.

Summary:

Background: A dysphoric mood is not required for the diagnosis of DSM-IV MDD. Individuals who deny depression, sadness, or feeling blue, may nonetheless be diagnosed with MDD if they have lost interest or pleasure in all, or almost all, of their usual activities, and experienced at least four other symptoms of depression. The underlying assumption is that depressed patients without low mood are no different than depressed patients who report dysphoric mood. In the present report from the Rhode Island Methods to Improve Diagnostic Assessment and Services (MIDAS) project we examined the validity of this assumption. **Methods:** We compared the demographic, family history, and clinical characteristics of patients who met the DSM-IV criteria for a current major depressive episode who did (n=839) and did not (n=63) report low mood. **Results:** Patients without depressed mood were significantly younger, and their current episodes were briefer, less severe, and associated with less suicidality and less psychosocial impairment. **Conclusion:** The results do not support DSM-IV's implicit assumption of no difference between depressed patients who do and do not report low mood. The alternative ways this might be addressed in future editions of the DSM will be discussed.

References:

1. Feighner JP, Robins, E, Guze, SB, Woodruff, RA, Winokur, G, Munoz, R (1972) Diagnostic criteria for use in psychiatric research. Arch Gen Psychiatry. 26:57-67.
2. Schatzberg AF, Rothschild, AJ (1992) Psychotic (delusional) major depression: Should it be included as a distinct syndrome in DSM-IV? Am J Psychiatry. 149:733-745.

NR310 Monday, May 22, 3:00 PM - 5:00 PM

Diagnosing MDD: Can the Clinical Utility of the *DSM-IV* Symptom Criteria Be Improved?

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Educational Objectives:

At the conclusion of this presentation the participant should be able to describe problems with the clinical utility of the DSM-IV symptom criteria for major depressive disorder and how a new definition improves upon the current official criteria.

Summary:

Background: There are two practical problems with the DSM-IV symptom criteria for MDD_they are somewhat lengthy and therefore difficult to remember, and there are difficulties in applying some of the criteria in patients with comorbid medical illnesses because of symptom nonspecificity. Therefore, in the present report from the Rhode Island Methods to Improve Diagnostic Assessment and Services (MIDAS) project we attempted to develop a briefer definition of major depression that is composed entirely of mood and cognitive symptoms. Our goal was to develop an alternative set of diagnostic criteria for major depression that did not include somatic symptoms but would nonetheless demonstrate a high level of concordance with the current DSM-IV definition. **Methods:** One thousand eight hundred psychiatric outpatients were evaluated with a semistructured diagnostic interview. We inquired about all of the DSM-IV diagnostic criteria for MDD for all patients. **Results:** After eliminating the somatic criteria from the DSM-IV MDD criteria and adding the symptom "reduced drive" there was a very high level of concordance with DSM-IV classification (95%). **Conclusions:** This new definition thus offers two advantages over the current DSM-IV definition_it is briefer and it is free of somatic symptoms thereby making it easier to apply with medically ill patients. We discuss using improvement in the clinical utility, rather than validity, of diagnostic criteria as the basis for making revisions in the nomenclature.

References:

1. First M, Pincus, H, Levine, J, Williams, J, Ustun, B, Peele, R (2004) Clinical utility as a criterion for revising psychiatric diagnoses. Am J Psychiatry. 161:946-954.
2. Kathol R, Noyes, J, R, Williams, J, Mutgi, A, Carroll, B, Perry, P (1990b) Diagnosing depression in patients with medical illness. Psychosom. 31:434-440.

NR311 Monday, May 22, 3:00 PM - 5:00 PM

Diagnosing MDD: Can a Self-Report Depression Questionnaire Be Used to Examine Questions About the *DSM-IV* Diagnostic Criteria?

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Educational Objectives:

At the conclusion of this presentation the participant should be able to describe how a self-report scale can be used to examine the performance of the symptom criteria for major depressive disorder.

Summary:

Background: This presentation is the final one in our series examining the DSM-IV diagnostic criteria for MDD. The data collected was part of the Rhode Island Methods to Improve Diagnostic Assessment and Services (MIDAS) project, a unique integration of a research assessment protocol into a community-based clinical practice. We were able to examine a number of psychometric and conceptual issues in the diagnosis of depression because we modified the diagnostic interview to inquire about all diagnostic criteria, as well as additional associated features, of all patients. The results reported in other presentations suggested that some changes in the diagnostic criteria might be warranted. However, before changes are made to the diagnostic nomenclature the results of any single study should be replicated. The cost of conducting this type of research is high, thereby reducing the likelihood of replication. As part of the MIDAS project we developed the Diagnostic Inventory for Depression (DID), a self-report scale that was specifically designed to assess the DSM-IV diagnostic criteria for MDD; thus, this scale could potentially be used to study many of the same questions examined in the present series, though at a fraction of the cost. In the present report we used the DID to examine questions that were addressed in three of the

prior reports in this series. The results of the present analysis based on the DID replicated the other reported findings based on the SCID. This suggests that a self-report measure such as the DID could be used in other settings to examine the issues studied in the present series, thereby facilitating the compilation of a more substantial literature upon which decisions regarding criteria modification could be based.

References:

1. Buchwald A, Rudick-Davis, D (1993) The symptoms of major depression. Journal of Abnormal Psychology. 102:197-205.
2. Zimmerman M, Sheeran, T, Young, D (2004) The Diagnostic Inventory for Depression: A self-report scale to diagnose DSM-IV for major depressive disorder. J Clin Psychol. 60:87-110.

NR312 Tuesday, May 23, 12:00 PM - 2:00 PM

Olanzapine Receptor Gene Polymorphisms and Depressive Symptom Response in Schizophrenia

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Educational Objectives:

At the conclusion of the session, the participant should be able to discuss genotypes associated with differences in depressive symptom response in acute olanzapine treatment of patients with schizophrenia.

Summary:

Introduction: Depression is frequently observed in patients with schizophrenia. Olanzapine has been associated with depressive symptom response in several psychiatric disorders, and depressive symptom response has been linked to antidepressant activity at several olanzapine neuroreceptor sites. Several genetic polymorphisms reportedly produce differential antidepressant response.

Method: We assessed response in 51 acutely psychotic patients with schizophrenia and Montgomery-Asberg Depression Scale (MADRS) scores ≥15, retrospectively genotyped for 64 single nucleotide polymorphisms (SNPs) of olanzapine neuroreceptor genes as well as other selected genetic polymorphisms with an *a priori* determined sequence of analysis. Baseline-to-endpoint reduction in MADRS over 6 weeks of olanzapine treatment was assessed by ANOVA.

Results: Olanzapine receptor SNPs associated with significant differences in depression response by genotypic analysis ($p \leq .05$) included alpha-1A adrenergic, alpha-2A adrenergic, dopamine-D1, dopamine-D2, and 5HT-6 receptor SNPs. None of the dopamine-D3, dopamine D4, histamine H2, 5HT-1A, 5HT-2A and 5HT-2C receptor SNPs assessed nor the 5HT transporter s/l alleles significantly influenced depressive symptom response. In addition, melanocortin-2 receptor SNPs were associated with differential response to olanzapine.

Conclusions: Specific olanzapine receptor gene SNPs predicted statistically and clinically significant depressive symptom reduction with olanzapine in substantial subsets of depressed patients with schizophrenia. Replication in other data sets is needed.

References:

1. Serretti A, Artioli P. From molecular biology to pharmacogenetics: a review of the literature on antidepressant treatment and suggestions of possible candidate genes. Psychopharmacology 2004;147:490-503.
2. Staddon S, Arranz MJ, Mancama D, Mata I, Kerwin RW. Clinical applications of pharmacogenetics in psychiatry. Psychopharmacology 2002;162:18-23.

NR313 Tuesday, May 23, 12:00 PM - 2:00 PM

Metabolic Syndrome Rates Among Patients With Schizophrenia Treated With Aripiprazole, Placebo, or Olanzapine

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Educational Objectives:

To demonstrate the effect of certain atypical antipsychotics on the rate of metabolic syndrome.

Summary:

Background: The recent CATIE publication (1) has demonstrated that patients with schizophrenia exhibit higher rates of metabolic syndrome (METs) compared with the general population. Since METs risk factors are exacerbated by use of certain antipsychotic medications (2), we compared rates of METs among patients with baseline METs who were subsequently randomized to either aripiprazole, placebo, or olanzapine.

Methods: The study sample consisted of patients from 4 pooled clinical trials of aripiprazole versus placebo and olanzapine with baseline METs (according to ATP-III criteria [3]). Rates of METs were then compared between treatment arms (aripiprazole-placebo, aripiprazole-olanzapine) at 26 weeks by Mantel-Haenzel Chi Square (LOCF, post hoc analysis).

Results: After 26 weeks of treatment in the placebo-controlled studies, METs rates were 41% for aripiprazole (n=141) versus 43% for placebo (n=73) (P=0.843). METs rates were 35% for aripiprazole (n=158) and 67% for olanzapine (n=141) in the comparative trials at 26 weeks (P=0.0002). Observed differences in the rates of METs between aripiprazole and olanzapine were driven primarily by component differences in waist circumference (P=0.002), triglyceride levels (P=0.0001) and HDL-C (P=0.02)

Conclusions: METs rates can be improved to levels comparable to placebo among patients treated with aripiprazole, but not for olanzapine patients. Weight and lipid variables appear to drive the difference in rates seen at 6 months. Given the high prevalence of METs in the schizophrenic population, therapies that decrease its incidence and severity should be given serious consideration.

References:

1. Lieberman J, Stroup S, McEvoy J, et al. Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. N Engl J Med 2005; 353:1209-1223.
2. Meyer JM, Koro CE. The effects of antipsychotic therapy on serum lipids: a comprehensive review. Schizophr Res 2004; 70:1-17.

NR314 Tuesday, May 23, 12:00 PM - 2:00 PM

Training for Assessment of Negative Symptoms of Schizophrenia Across Languages and Cultures Using the Negative Symptom Assessment (NSA) Scale

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to:

1. Describe the Negative Symptom Assessment (NSA) Scale.
2. Compare results of training on the NSA versus the Positive and Negative Syndrome Scale in terms of achieving acceptable agreement among raters across different nationalities and languages.

Summary:

Background: Lack of agreement among raters in international trials is a source of nonspecific variance that may diminish statistical power and increase the number of patients required for a valid study. The Negative Symptom Assessment (NSA) scale, a 16-item clinician-rated instrument for use in patients with schizophrenia, has shown reliability and validity in English-speaking raters. We analyzed the level of agreement achieved among raters of multiple nationalities and languages using the NSA versus the Positive and Negative Syndrome Scale (PANSS).

Methods: Two cohorts of international clinical trial investigators were enrolled: 120 from the US and 180 from 18 other countries. Enrollees viewed ≥1 training lecture, rated ≥1 videotaped semi-structured NSA interview of a schizophrenic patient, and received detailed feedback on proper rating methods. Both cohorts received similar training for the PANSS. Most raters were unfamiliar with the NSA before training but had previous PANSS experience. Raters were then evaluated on their rating of another videotaped patient interview. Acceptable rater agreement was a score within 1 point of the cohort modal score on ≥80% of the rating instrument items.

Results: Using the NSA, acceptable agreement was achieved by 85/90 (94%) of US raters versus 174/180 (97%) of non-US raters (P=0.38). In contrast, using the PANSS, agreement was achieved by 104/120 (87%) of US raters versus 168/173 (97%) of non-US raters (P=0.0009).

Conclusions: A high level of agreement in rating the NSA was found among raters across multiple countries. The US and international cohorts achieved comparably high rates of success in NSA training, whereas in PANSS training the cohorts showed a significant difference in success rates. This suggests that raters can be more efficiently and reliably trained to assess negative symptoms using the NSA across many languages and cultures.

Funding Source: This study was supported by Organon Laboratories Ltd and Pfizer Inc.

References:

1. 1. Axelrod BN, Goldman RS, Alphs, LD: Validation of the 16-item Negative Symptom Assessment. J Psychiatr Res 1993; 27:253-258.
2. 2. Eckert SL, Diamond PM, Miller AL, Velligan DI, Funderburg LG, True JE: A comparison of instrument sensitivity to negative symptom change. Psychiatry Res 1996; 63:67-75.

NR315 Tuesday, May 23, 12:00 PM - 2:00 PM

Identifying subgroups with good and poor response in placebo-controlled trials in schizophrenia

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Educational Objectives:

To introduce viewers to an innovative method for characterizing subgroups of good and poor responders in clinical trials, and to demonstrate the use of this method in the analysis of response in pooled data from four placebo-controlled trials of ziprasidone in schizophrenia.

Summary:

Objective: To identify characteristics of subgroups with good or poor response in placebo-controlled trials of ziprasidone in schizophrenia.

Method: Active region finder (ARF) analysis_an innovative method of data mining that focuses on high-activity regions_was performed on data sets from four randomized, placebo-controlled trials of ziprasidone in patients (n = 951) with acute exacerbation of schizophrenia (dose range, 10 to 200 mg/day). The primary outcome measure was the BPRS total score, controlling for baseline BPRS score. Predictors included age, gender, race, protocol, dose, illness duration, smoking status, and baseline ratings from several standardized instruments (PANSS, CGI-S, AIMS). Separate trees were produced for good and poor responses.

Results: Dose was the most powerful predictor in the "good response" tree, with the best response noted in patients receiving ziprasidone 120 or 160 mg/day and having a short duration of illness. Presence of abnormal movements produced the first split in the "poor response" tree (ie, was the strongest predictor of poor response).

Conclusions: ARF analyses successfully identified subgroups with good or poor response and were particularly useful in identifying nonlinear associations between predictors and response.

References:

1. Amaratunga D, Cabrera J: Mining data to find subsets of high activity. Journal of Statistical Planning and Inference 2004; 122:23-41.
2. Daniel D.G., Zimbroff D.L., Potkin S.G., et al: Ziprasidone 80 mg/day and 160 mg/day in the acute exacerbation of schizophrenia and schizoaffective disorder: a 6-week placebo-controlled trial. Neuropsychopharmacology 1999; 20:491-505.

NR316 Tuesday, May 23, 12:00 PM - 2:00 PM

Psychopathology and Risk for CHD in Psychotic Patients: The Clamors Study

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Educational Objectives:

At the end of this presentation, the participant should be able to recognize the association between the severity of psychopathology and the risk for coronary heart disease in the treatment of psychotic patients with antipsychotics.

Summary:

Aim: To determine the relation between the severity of psychopathology and coronary heart disease (CHD) risk in schizophrenic patients treated with antipsychotics.

Methods: Retrospective, cross-sectional, multicenter study where 117 Spanish Psychiatrists (The CLAMORS Collaborative Group) recruited consecutive outpatients meeting DSM-IV criteria for Schizophrenia, Schizophreniform or Schizoaffective Disorder, under antipsychotic treatment for at least 12 weeks. Clinical severity was assessed by PANSS and CGI scales, and CHD risk by SCORE (10-year CV death) and Framingham (10-year all CV events) equations. Multivariate logistic regression models were applied.

Results: 1452 evaluable patients (863 men, 60.9%), 40.7±12.2 years (mean±SD), were included. The overall 10-year risks were 0.9±1.9 (mean±SD) and 7.2±7.6 for SCORE and Framingham, respectively. 8%(95%CI:6.5-9.5) and 22.1%(95%CI:20.0-24.3) of patients showed high/very high risk according to SCORE (>=3%) and Framingham (>=10%) equations. More patients with higher

PANSS score (>68, median score) showed high/very high risk with SCORE and Framingham scoring: 10.6%(95%CI:8.0-13.1) versus 6.2%(95%CI:4.6-8.4), p<0.05; and 27.6%(95%CI:24.2-31.1) versus 17.8%(95%CI:15.0-20.6), respectively, p<0.05. More patients with higher CGI scores showed high/very high risk.

Conclusions: CHD risk was higher among psychotic patients treated with antipsychotics with more severe psychopathology: the more severe psychopathology the higher the risk.

On behalf of the CLAMORS Collaborative Group.

References:

1. Goff DC: A comparison of ten-year cardiac risk estimates in schizophrenia patients from the CATIE study and matched controls. Schizophr Res 2005; 80(1):45-53.
2. Glassman AH: Schizophrenia, antipsychotic drugs, and cardiovascular disease. J Clin Psychiatry 2005; 66(suppl 6):5-10.

NR317 Tuesday, May 23, 12:00 PM - 2:00 PM

Psychopathology and MS in Psychotic Patients: The Clamors Study

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Educational Objectives:

At the end of this presentation, the participant should be able to recognize the association between the severity of psychopathology and the prevalence of metabolic syndrome in the treatment of psychotic patients with antipsychotics.

Summary:

Aim: To determine the relation between the severity of psychopathology and prevalence of metabolic syndrome (MS) in patients treated with antipsychotics.

Methods: Retrospective, cross-sectional, multicenter study where 117 Spanish Psychiatrists (The CLAMORS Collaborative Group) recruited consecutive outpatients meeting DSM-IV criteria for Schizophrenia, Schizophreniform or Schizoaffective Disorder, under antipsychotic treatment for at least 12 weeks. Clinical severity was assessed by PANSS and CGI. MS was defined by at least 3 of the following components: waist circumference>102(men)/ >88(women)cm; tryglicerides>=150mg/dL; HDL-cholesterol= 110mg/dL. Multivariate logistic regression models were applied.

Results: 1452 evaluable patients (863 men, 60.9%), 40.7±12.2years (mean±SD) were included. MS was presented in 24.6%[23.6%(men), 27.2%(women); p=0.130)]. After adjustment, age [>40years(men)/45years (women)] and schizophrenic symptoms severity (PANSS>68, median value) were associated with higher MS risk [OR95%CI: 1.82(1.42-2.33) and 1.66(1.29-2.13), respectively]. More patients with higher PANSS score (>68) showed MS: 29.7%(95%CI:5.2-54.3) versus 20.0%(95%CI:6.8-46.0), p<0,001. Abdominal obesity, hypertrygliceridemia, hypertension and glucose intolerance were more prevalent in patients with higher PANSS: 39.4%(95%CI:35.6-43.2) versus 46.3%(95%CI:42.3-50.4), 33.3%(95%CI:29.7-37.0) versus 41.1(95%CI:37.1-45.0), 49.9%(95%CI:44.4-55.5) versus 58.4%(95%CI:52.7-64.1), 11.2%(95%CI:6.5-15.9) versus 17.9%(95%CI:12.1-23.7), respectively, p<0.05. More patients with higher CGI scores showed MS.

Conclusions: MS prevalence was higher among schizophrenic patients treated with antipsychotics with more severe psychopathology.

On behalf of the CLAMORS Collaborative Group.

References:

1. McEvoy JP:Prevalence of the MS in patients with schizophrenia:Baseline results from the Clinical AP Trials of Intervention Effectiveness (CATIE) schizophrenia trial and comparison with national estimates from NHANES III. Schizophr Res 2005;80(19-32).
2. Meyer JM: Antipsychotic Trials of Intervention Effectiveness (CATIE) Schizophrenia Trial: Clinical comparison of subgroups with and without the metabolic syndrome. Schizophr Res 2005; 80(1):9-18.

NR318 Tuesday, May 23, 12:00 PM - 2:00 PM

Suicidality in Patients With FRBD Treated With Long-Acting Risperidone

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Educational Objectives:

At the conclusion of this presentation, participants will be familiar with the measurement of suicidal thinking and its response to treatment with a long-acting, atypical antipsychotic in patients with frequently relapsing bipolar disorder (FRBD).

Summary:

Objective: This trial evaluates the effect of long-acting risperidone (LAR) on mood symptoms and suicidal thinking in patients with frequently relapsing bipolar disorder (FRBD).

Methods: Patients meeting criteria for BD, and experiencing ≥4 episodes requiring clinical intervention in the past 12 months and ≥2 episodes in the past 6 months, received open-label (OL) augmentation of treatment-as-usual with LAR (25-50 mg) for 16 weeks. Remitters (both Young Mania Rating Scale [YMRS] ≤10 and Montgomery-Asberg Depression Rating Scale [MADRS] ≤10 over the last 4 weeks of the OL phase) were eligible for randomization to placebo or LAR in a double-blind (DB), 52-week, relapse-prevention phase. Measures of suicidal thinking included the InterSePT Scale for Suicidal Thinking-Revised (ISST-R, range 0-24) and the MADRS-Item 10 (MADRS-10; range 0 to 6).

Results: ISST-R data at OL baseline and endpoint were available for 77 of the first 84 subjects enrolled. Mean (±SD) change score for ISST-R was -0.4 ± 1.9 (P <0.049). Of 20 subjects with suicidal ideation (ISST-R ≥1) at baseline, 16 showed a decrease in ISST-R score (range, -9 to -1), 3 showed no change, and 1 showed an increase (of 5). The mean (± SD) absolute and percentage changes among these 20 patients were -2.3 ± 3.0 (P = 0.003) and -69 ± 66 (P <0.001), respectively. Of the 57 patients without baseline suicidal ideation (ISST-R = 0), 53 (93%) maintained ISST-R = 0, and 4 (7%) showed increases in ISST-R scores (range, 2 to 3). Mean (±SD) change score for MADRS-10 in all subjects was -0.4 ± 1.0 (P <0.002).

Conclusions: Preliminary OL findings suggest treatment with LAR may reduce suicidal thinking in FRBD. DB data, when available, will inform us on the validity of these observations.

Source of Funding: Janssen, L.P.

References:

1. Leverich GS, Altshuler LL, Frye MA, Suppes T, Keck PE Jr, McElroy SL, Denicoff KD, Obrocea G, Nolen WA, Kupka R, Walden J, Grunze H, Perez S, Luckenbaugh DA, Post RM: Factors associated with suicide attempts in 648 patients with bipolar disorder in t.
2. Baldessarini RJ, Tondo L: Suicide risk and treatments for patients with bipolar disorder. JAMA 2003; 290:1517-1519 Erratum in: JAMA 2004; 291:186.

NR319 Tuesday, May 23, 12:00 PM - 2:00 PM

Cognitive and Functional Improvement With Long-Acting Risperidone Treatment

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the correlation between cognitive and functional improvements in patients with schizophrenia receiving long-acting injectable risperidone.

Summary:

Background: Cognitive deficits are commonly noted in patients with schizophrenia. Patients receiving atypical antipsychotics, including risperidone, have shown improved cognition and independent role functioning. This report examines correlations between cognition and functioning in patients treated with long-acting risperidone.

Methods: Data are from a prospective, randomized, double-blind, international, 52-week study of stable patients with schizophrenia or schizoaffective disorder receiving long-acting, injectable risperidone (25 or 50 mg every 2 weeks). Patients completed a computer-administered cognitive battery at multiple time points. Correlation analyses were performed to assess relationships between the neurocognitive composite score (NCS) and 7 cognitive domains (processing speed, attention and impulsivity, working memory, declarative memory, visual memory, executive function, and social cognition), with Positive and Negative Syndrome Scale (PANSS) total, PANSS factors, Personal and Social Performance scale (PSP), and Strauss-Carpenter Level of Functioning (LOF) scores.

Results: Improvements from baseline were seen in the NCS and 6 cognitive domains (processing speed, attention and impulsivity, declarative memory, visual memory, executive function, and social cognition) at endpoint. Significant, but weak, correlations were observed at endpoint between improvements in 5 cognitive domains (processing speed, attention, working memory, declarative memory, and social cognition), and PSP, LOF, and PANSS total scores (each $P < 0.05$). Significant, but weak, correlations were also observed between the same 5 cognitive domains and the disorganized-thoughts factor and PANSS negative-symptom factor (each $P < 0.05$), although not for other PANSS subscales (anxiety/depression, PANSS positive, and uncontrolled hostility factors).

Discussion: Cognitive functioning improved significantly in multiple domains in clinically stable patients receiving maintenance treatment with long-acting risperidone. These improvements correlate weakly with improvements in patient functioning and symptoms. Data suggest that changes in cognitive function may not be strongly correlated with clinical improvement in stable patients, or that a temporal relationship, undetected here, exists between these variables.

Source of Funding: Janssen, LP.

References:

1. Addington J, Addington D: Neurocognitive and social functioning in schizophrenia: a 2.5 year follow-up study. Schizophr Res 2000; 44:47-56.

2. Meltzer HY, McGurk SR: The effects of clozapine, risperidone, and olanzapine on cognitive function in schizophrenia. Schizophr Bull 1999; 25:233-255.

NR320 Tuesday, May 23, 12:00 PM - 2:00 PM

Coronary Heart Disease (CHD) Risk in Psychotic Patients: The Clamors Study

Julio Bobes, Ph.D. *University of Oviedo, Medicine Department, Psychiatry Area, Julian Claveria, 6, Oviedo, 33006, Spain*, Celso Arango, Ph.D., Rafael Carmena, Ph.D., Pedro Aranda, Ph.D., Margarida Garcia-Garcia, M.S.C., Javier Rejas, Ph.D.

Educational Objectives:

At the end of this presentation, the participant should be able to recognize the risk for coronary heart disease in the treatment of psychotic patients with antipsychotics.

Summary:

Aim: To document CHD risk in psychotic patients treated with antipsychotics.

Methods: Retrospective, cross-sectional, multicenter study where 117 Spanish Psychiatrists (The CLAMORS Collaborative Group) recruited consecutive outpatients meeting DSM-IV criteria for Schizophrenia, Schizophreniform or Schizoaffective Disorder, under antipsychotic treatment for at least 12 weeks. CHD risk was assessed by SCORE (10-year CV death) and Framingham (10-year all CV events) equations. Multivariate logistic regression models were applied.

Results: 1452 evaluable patients (863 men, 60.9%), 40.7±12.2 years (mean±SD), were included. The overall 10-year risks were 0.9±1.9 (SCORE) and 7.2±7.6 (Framingham). 8%(95%CI:6.5-9.5) and 22.1%(95%CI:20.0-24.3) of patients showed high/very high risk according to SCORE (>3%) and Framingham (>10%). More males showed high/very high risk (SCORE and Framingham): 9.9%(95%CI:7.8-12.0) versus 5.2%(95%CI:3.3-7.2), p= 0.002; and 27.7%(95%CI:24.7-30.7) versus 13.5%(95%CI:10.7-16.4), p<0.001, respectively. Age, ICG severity and PANSS scales were positively associated with CV death and CV events risk. Compared with haloperidol, only ziprasidone was more likely to have lower risk (<10%) for CV events [adjusted odds ratio (95%CI): 1.81(1.06-3.10), p=0.031].

Conclusions: CHD risk was found higher among psychotic patients treated with antipsychotics than in the general population. Age, sex, poor disease control and antipsychotic treatment could be associated with CHD risk.

On behalf of the CLAMORS Collaborative Group.

References:

1. Goff DC: A comparison of ten-year cardiac risk estimates in schizophrenia patients from the CATIE study and matched controls. Schizophr Res 2005; 80(1):45-53.

2. Glassman AH: Schizophrenia, antipsychotic drugs, and cardiovascular disease. J Clin Psychiatry 2005; 66(suppl 6):5-10.

NR321 Tuesday, May 23, 12:00 PM - 2:00 PM

Metabolic Syndrome (MS) in Psychotic Patients: The Clamors Study

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Educational Objectives:

At the end of this presentation, the participant should be able to recognize the risk for metabolic syndrome in the treatment of psychotic patients with antipsychotics.

Summary:

Aim: To assess the prevalence of MS in patients treated with antipsychotics.

Methods: Retrospective, cross-sectional, multicenter study where 117 Spanish Psychiatrists (The CLAMORS Collaborative Group) recruited consecutive outpatients meeting DSM-IV criteria for Schizophrenia, Schizophreniform or Schizoaffective Disorder, under antipsychotic treatment for at least 12 weeks. MS was defined by at least 3 of the following components: waist circumference >102(men)/>88(women)cm; tryglicerides>=150mg/dL; HDL-cholesterol=110mg/dL. Multivariate logistic regression models were applied.

Results: 1452 evaluable patients (863 men, 60.9%), 40.7±12.2 years (mean±SD) were included. MS was presented in 24.6% [23.6%(men), 27.2%(women); p=0.130)]. After adjustment, age [>40years(men) / 45years(women)] and severity of schizophrenic symptoms (PANSS>median value) were associated with higher risk of MS [Odds ratios (95%CI); 1.82(1.42-2.33) and 1.66(1.29-2.13), respectively]. Abdominal obesity and low HDL-cholesterol were more prevalent in women: 54.5%(95%CI:50.2-58.9) versus 34.3%(95%CI:31.0-37.7), and 46.1%(95%CI:41.4) versus 28.5(95%CI:50.8), p<0.001 in both cases, respectively. Hypertension and hipertrygliceridemia were more prevalent in men: 59.0%(95%CI:55.7-62.3) versus 46.0%(95%CI:41.8-50.2), and 40.7%(95%CI:37.2-44.2) versus 32.4(95%CI:28.3-36.5), p<0.01 in both cases respectively.

Conclusions: Compared with the general population, MS prevalence was higher among schizophrenic patients treated with antipsychotics, showing a value similar to that of general population ten to fifty years older.

On behalf of the CLAMORS Collaborative Group.

References:

1. McEvoy JP:Prevalence of the MS in patients with schizophrenia:Baseline results from the Clinical AP Trials of Intervention Effectiveness (CATIE) schizophrenia trial and comparison with national estimates from NHANES III. Schizophr Res 2005;80(19-32).
2. Meyer JM: Antipsychotic Trials of Intervention Effectiveness (CATIE) Schizophrenia Trial: Clinical comparison of subgroups with and without the metabolic syndrome. Schizophr Res 2005; 80(1):9-18.

NR322 Tuesday, May 23, 12:00 PM - 2:00 PM

Remission of Schizophrenia Symptoms Associated With Functional Improvement

Cynthia Bossie, Ph.D. *Janssen Pharmaceutica, Inc., Medical Affairs, 1125 Tranton-Harbourton Road, Titusville, NJ, 08560*, Georges Gharabawi, M.D., Stephen C. Rodriguez, M.S., Ibrahim Turkoz, M.S., Kristin Dragotta, Pharm.D., George M. Simpson, M.D.

Educational Objectives:

At the end of this presentation, participants should recognize that remitted patients, as defined by both duration and severity criteria, have improved function and insight, compared to nonremitted patients.

Summary:

Objective: Recently defined criteria for remission in schizophrenia highlight expanded treatment goals. We evaluated how meeting remission criteria corresponded to ratings of patient status.

Methods: We completed a post hoc analysis of a 1-year, double-blind study of stable patients with schizophrenia or schizoaffective disorder receiving long-acting, injectable risperidone 25 or 50 mg every 2 weeks. Remission criteria applied were: absent to mild symptoms on 8 core Positive and Negative Syndrome Scale items for ≥6 months.

Results: Although patients were clinically stable, 61.4% (n=194) did not meet baseline remission severity criteria. Among these, 21.6% (n=42) met remission criteria (severity and duration components) during the study; 90.0% of remitted patients completed the study. Remitted patients experienced low rates of protocol-defined relapse (n=1; 2.4%) and improved overall clinical status by Clinical Global Impressions of Severity ratings of not ill to mildly ill (21.4% at baseline and 88.1% at endpoint). Significant improvements were seen in mean (± SD) Personal and Social Performance (60.6±14.1 to 71.5±10.9; *P*<0.001) and Strauss-Carpenter Levels of Functioning (22.0±5.2 to 23.5±5.0; *P*=0.05) scores. Some, although lesser, improvements were noted in nonremitters. Mean (±SD) insight scores were 2.7 (0.98), baseline, and 2.1 (0.87), endpoint in remitters, and remained 2.8 at baseline and endpoint in nonremitters. Most commonly reported (≥15%) adverse events were headache (26%) and insomnia (26%) for remitted patients, and psychiatric disorder NOS (28%), insomnia (26%), anxiety (17%), and headache (16%) for nonremitted patients.

Conclusions: These findings link these remission criteria, utilizing both severity and duration criteria, with improvement in functioning and insight.

Sponsored by Janssen, LP.

References:

1. Andreasen NC, Carpenter W, Kane JM, Lasser RA, Marder SR, Weinberger DR. Remission in schizophrenia: proposed criteria and rationale for consensus. Am J Psychiatry 2005; 162:441-449.
2. Simpson G, Lasser RA, Bossie CA, Rodriguez S, Turkoz I, Gharabawi G. Maintenance of effect with long-acting risperidone: A one-year double-blind comparison of two doses in patients with schizophrenia or schizoaffective disorder. J Clin Psych. In prep.

NR323 Tuesday, May 23, 12:00 PM - 2:00 PM

Physical Health Parameters in Patients with Severe Mental Illness: Baseline data from the Well-Being Support Programme in UK

David Yeomans *Leeds*, Shubalade Smith, chris bushe, M. Eriksson, Gary Sullivan, Oatway Helen

Educational Objectives:

Educational Objectives: At the end of this presentation participants will be aware of the extent of physical illness and cardiovascular risk factors present in UK SMI (severe mental illness) patients. Current evidence in UK suggests that much of this pathology may be undiagnosed.

Summary:

Introduction: Much excess mortality in severe mental illness (SMI) is attributable to natural causes (cardiovascular and respiratory). Evidence suggests that risk factors for physical illness are not routinely measured.

Method: In the UK, seven geographically varied centres were assigned a nurse to monitor physical health of SMI patients in the "Well-Being Support programme" (WSP). A physical health screen was performed.

Results: 966 outpatients with SMI > 2 years enrolled. Prior to WSP 31% patients received physical health checks with wide variation across the 7 centres. Mean BMI 31, 81%>25, 49%>30 and 24% >35. Mean BP 132/82 with 50% patients having hypertension or pre-hypertension. No physical activity was done by 34%. Abnormal liver enzymes were found in 50%. Random glucose > 7.1 mmol/l was found in 17.9%. Significant associations were found between BMI and diastolic BP, diet and self-esteem. Dyslipidaemia was found in 71%. BMI >35 was significantly more common in females 30% than males 18%.

Conclusion: Physical health problems are a common finding in SMI patients. The WSP provided a screening and management

option for SMI patients who currently do not receive adequate physical health care. There is potential to address many preventable cardiovascular risk factors.

References:

1. Bushe C, Haddad P, Peveler R and Pendlebury J (2005) The role of lifestyle interventions and weight management in schizophrenia. Journal of Psychopharmacology (suppl) 19: 28-35.
2. Brown S, Birtwistle J, Roe L, Thompson C (1999) The unhealthy lifestyle of people with schizophrenia. Psychol Med 29: 697-701.

NR324 Tuesday, May 23, 12:00 PM - 2:00 PM

A Randomized, Double-Blind, Pilot Trial of Switching to Quetiapine vs. Risperidone Continuation in Outpatients With Risperidone-Associated Sexual Dysfunction

Matthew J. Byerly, M.D. *UT Southwestern Medical Center at Dallas, 5323 Harry Hines Blvd, Dallas, TX, 75390*, Paul Nakonezny, Ph.D., Rhiannon Bugno, B.A., Jason Boles, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to compare the effects of switching to quetiapine vs. risperidone continuation on sexual functioning in outpatients with risperidone-associated sexual side effects.

Summary:

Introduction: Preliminary data suggest risks of sexual side effects in patients with schizophrenia may be reduced by switching from risperidone to quetiapine therapy.

Objective: Compare the effects of switching to quetiapine versus risperidone continuation on sexual functioning in outpatients with risperidone-associated sexual side effects.

Methods: Outpatients (n=44, age ≥18 years) with schizophrenia/schizoaffective disorder who experienced risperidone-associated sexual dysfunction were randomized to 6 weeks of double-blind risperidone continuation (6 mg/day maximum allowable) or switching to quetiapine (to 300 mg/day, Week 1; 800 mg/day maximum allowable, Weeks 3-6). The 5-item Arizona Sexual Experience Scale (ASEX) assessed sexual functioning at baseline and Weeks 1, 2, 4 and 6. Mixed-model analysis of repeated measures included gender and baseline ASEX and PANSS scores as covariates.

Results: Twenty of 22 patients who continued on risperidone and 18 of 22 patients who switched to quetiapine were assessed at Week 6. There was no significant Group effect for ASEX total scores (p=0.78) and ASEX sub-items (p's>0.13) and no Group × Period interaction for ASEX total scores (p=0.66) and ASEX sub-items (p's>0.11). Treatment Group effects on ASEX total scores were not significantly different in any prospective weeks (p's>0.55). Adjusted average ASEX total scores were slightly lower in the quetiapine switch than risperidone continuation group at Weeks 2 and 6 (20.81 versus 21.85 and 18.96 versus 20.19, respectively; Cohen's d=0.17 and 0.19, respectively).

Conclusions: In this pilot trial, ASEX scores did not differ significantly between outpatients switching to quetiapine versus continuing risperidone, although the quetiapine switch group had lower adjusted ASEX scores at Weeks 2 and 6.

Supported by funding from AstraZeneca Pharmaceuticals LP.

References:

1. Arnt J, Skarsfeldt T. Do novel antipsychotics have similar pharmacological characteristics? A review of the evidence. Neuropsychopharmacology 1998;18(2):63-101.
2. Byerly MJ, et al. An empirical evaluation of the Arizona sexual experience scale and a simple one-item screening test for assessing antipsychotic-related sexual dysfunction in outpatients with schizophrenia and schizoaffective disorder. Schizophr Res.

NR325 Tuesday, May 23, 12:00 PM - 2:00 PM

Assessing Hyperglycemia-Related AEs in Patients Receiving Aripiprazole for Psychotic and Nonpsychotic Disorders

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to list common hyperglycemia-related adverse events (including diabetes mellitus) associated with the use of certain antipsychotic medications. The participant should also be aware that pooled data from 13 placebo-controlled trials of patients with schizophrenia, bipolar mania, or psychosis associated with Alzheimer's disease showed that aripiprazole is an effective treatment that is not associated with increased incidence of hyperglycemia-related adverse events or diabetes mellitus.

Summary:

Objective: Assess incidence of hyperglycemia-related AEs (H-AEs) in a pooled safety population from 13 randomized, double-blind, placebo-controlled trials of aripiprazole 2-30mg/d for schizophrenia, bipolar mania, or psychosis associated with Alzheimer's disease (AD).

Methods: Subjects treated with aripiprazole 2-30mg/d (n=1911) or placebo (n=1225) were pooled from five short-term 4-6-week schizophrenia trials, one long-term (26-week) schizophrenia trial, five 3-week bipolar mania trials, and two 10-week psychosis of AD trials. The H-AEs identified in these trials were diabetes mellitus (DM), hyperosmolar coma, ketosis, diabetic ketosis, hyperglycemia, glycosuria, and decreased glucose tolerance. Incidences of fasting glucose levels ≥126mg/dL, random glucose levels ≥200mg/dL, or elevated glycosylated hemoglobin were also assessed. Statistical differences were analyzed by ANCOVA.

Results: Across all studies, 0.37% of aripiprazole- versus 0.49% of placebo-treated patients experienced H-AEs (hazard ratio [HR]=0.65 in favor of aripiprazole; 95% CI=0.22-1.98). No serious H-AEs were observed. Pooled rates of DM were 0.16% for aripiprazole- versus 0.24% for placebo-treated patients (HR= 0.49 in favor of aripiprazole; 95% CI=0.10-2.44). All reports of DM occurred in patients with prior history of DM. In the short-term schizophrenia trials, incidences of DM or H-AEs were: aripiprazole (0.22%, 0.54%), placebo (0.48%, 0.48%), respectively. There were no reports of treatment-emergent DM or H-AEs in the long-term schizophrenia trial. In the bipolar trials, incidences of DM or H-AEs were: aripiprazole (0.17%, 0.17%), placebo (0.23%, 0.46%), respectively. In the AD trials, incidences of H-AEs were: aripiprazole (0.43%), placebo (0.90%) (no reports of treatment-emergent DM). Incidences of elevated fasting glucose (n=989) and glycosylated hemoglobin (n=1397) were significantly lower for aripiprazole than placebo (10.5% versus 15.5% and 9.1% versus 12.8%, respectively; P≤0.05 for both).

Conclusion: Multiple placebo-controlled trials show that aripiprazole is not associated with increased risk of hyperglycemia-related AEs or diabetes mellitus.

References:

1. Cohen D, Dekker JJ, Peen J, et al: Prevalence of diabetes mellitus in chronic schizophrenic inpatients in relation to long-

term antipsychotic treatment. Eur Neuropsychopharmacol October 28, 2005. [Epub ahead of print].

2. Marder SR, McQuade RD, Stock E, et al: Aripiprazole in the treatment of schizophrenia: safety and tolerability in short-term, placebo-controlled trials. Schizophr Res 2003; 61:123-136.

NR326 Tuesday, May 23, 12:00 PM - 2:00 PM

DSM Criteria for Catatonic Schizophrenia Lack Concurrent Validity

Brendan T. Carroll, M.D. *Neuroscience Alliance, Neuropsychiatry, The Neuroscience Alliance, 330 Taylor Blair Road, West Jefferson, OH, 43162*, Harold W. Goforth, M.D., Joseph W. Y. Lee, M.D., Christopher Thomas, Pharm.D., Arthur Thalassinos, M.D., RaeAnn Kirchoffer, B.S., Michelle Bell, B.A.

Educational Objectives:

The participant should be able to distinguish catatonic signs from symptom based criteria in the diagnosis of catatonic schizophrenia. The participant should be able to recognize the low concurrent validity of terms used to describe catatonia.

Summary:

The objective of this study was to identify the terminology used in the diagnostic criteria for catatonic schizophrenia. These criteria have been a concern for the Catatonia Consortium, a freestanding department of clinicians and researchers in the field of motility psychoses. Methods: We reviewed the criteria and terminology used in DSM-IV and DSM-IV-TR for catatonia and identified in one rating scale and 1 book written on the subject. We also examined the issue of the clinical interview versus a neurocognitive motor exam to detect catatonic signs. Results: We found 29 terms used in the to the diagnosis of the catatonic subtype. Clear and unambiguous descriptions of terms were as follows: DSM-IV-TR= 6 (20.7%), Bush-Francis Scale=26 (89.7%), Fink & Taylor=12 (41.4%). A field test of these criteria reveals that graduate level interviewers were unable to detect catatonic signs in the absence of a limited clinical examination. Discussion: Our findings support the use of a motor rating scale with clearly defined terms to diagnose catatonic schizophrenia. Catatonic signs must be detected by exam and cannot be identified by clinical interview alone. We found low concurrent validity in criteria terminology and suggest that a new approach to DSM-V for this disorder is warranted.

References:

1. Bush G, Fink M, Petrides G, et al. Catatonia I: Rating scale and standardized examination. Acta Psychiatr Scand 1996; 93:129-136.
2. Fink M, Taylor MA. Catatonia: A Clinician's Guide to Diagnosis and Treatment, Cambridge, UK, Cambridge University Press, 2003.

NR327 Tuesday, May 23, 12:00 PM - 2:00 PM

Clinical Profiles in Delusional Disorder: A Descriptive Study Based on a Large Spanish Case Register

Enrique de Portugal, M.D. *Madrid, Spain*, Nieves C. Gonzalez, M.S.C., Josep M Haro, M.D., Jorge A. Cervilla, M.D.

Educational Objectives:

At the end of this presentation, the audience should be able to have got acquainted with the following concepts:

1) The estimated community-care based prevalence of delusional disorder

2) The prevalence of delusional disorders subtypes

3) The sociodemographic correlates of delusional disorder

4) The environmental adversity associated to delusional disorder in this sample

5) The psychotic phenomenology of delusional disorder both in general and compared among subtypes

6) The description of symptomatic clusters associated with Delusional Disorder emerged via principal component factor analysis

Summary:

Objective: Few empirically-based studies on delusional disorder (DD) exist. We aim to: 1) Estimate psychiatric-care prevalence of delusional disorder; 2) Describe sociodemographic, and clinical correlates of DD; and, 3) Identify clinical profiles associated to DD and its subtypes.

Methods: This is a case register study based on all those subjects attending community mental health services within a geographically well-defined area. 463 patients had been diagnosed as DD cases at psychiatric services serving a catchment area of some 600.00 inhabitants living in Barcelona (Spain) during a three year period (2001, 2002 and 2003). A thorough systematic review of computerised medical records was used to establish DSM-IV-TR diagnosis, rendering a final valid sample of 370 DD patients. Independent variables collected include: sociodemographic data, family and personal psychiatric history, comorbid diagnoses on all DSM-IV axes (including GAF).We used descriptive and univariate statistical methods to explore sample frequencies and compare covariates among DD subtypes. We also used PCA to extract clinical profiles showing Eigenvalue over 1.5.

Results: 56.5% female, mean age 55, mean GAF 51. The estimated community-care prevalence of DD is 0.06%. Most frequent subtypes were: persecutory (48%), Jealous (11%), Mixed (11%) and somatic (5%) (23%were NOS). Most frequent symptoms were: self-reference (40%), irritability (30%), depressive (20%) and aggressiveness (15%). Hallucinations were present in 16% (6% tactile; 4% olfatory). Nearly 9% had a family history of schizophrenia (higher among those with the jealous subtype -p=0.013), 42% had a comorbid axis II diagnosis (mostly paranoid). Depression was more frequent among the persecutory and jealousy types (p=0.024). Functioning was significantly better among jealous and mixed types and worse amongst Extended Release otomaniac and grandious cases (p=0.008). We identified 3 clinical dimensions: hallucinatory, affective and relational.

Conclusions: Prevalence of DD seems higher than previously reported. We find novel significant clinical correlates with DD in a large sample.

References:

1. Kendler, K. Demography of Paranoid Psychosis (Delusional Disorder) - A review and Comparison With Schizophrenia and Affective-Illness.
2. Kendler, KS Hays, P. Paranoid Psychosis (Delusional Disorder) and Schizophrenia. Archives of General Psychiatry. 1981. 38, 547-551.

NR328 Tuesday, May 23, 12:00 PM - 2:00 PM

Gender selection bias in antipsychotic trials

Ana C. Chaves, M.D. *Federal University of Sao Paulo, Psychiatry, Rua Haroldo Veloso 411 apt 81, Sao Paulo, 04533080, Brazil*, Mary V. Seeman, M.D.

Educational Objectives:

At the conclusion of this presentation the participant would be able to identify factors related to gender selection bias in RCTs of the newer antipsychotics in schizophrenia and related disorders.

Summary:

Context: The sex prevalence of schizophrenia is approximately equal and yet clinical trials of new therapeutic drugs have been conducted, for the most part, on men.

Objective: To review the percentage of women in schizophrenia clinical trials of the new "atypical" antipsychotic medications.

Data Source: MEDLINE and Cochrane databases were searched for English-language RCTs involving risperidone, olanzapine, quetiapine, ziprasidone and aripiprazole.

Study Selection: English language RCTs with a sample size over 50 and a subject diagnosis of schizophrenia, schizophrenia spectrum disorder or broad psychosis were included for review. Trials that included treatment-resistant patients, or where clozapine was one of the comparator drugs, or that enrolled only mood disorders patients or only patients from Veteran Affairs Centers were excluded.

Data Extraction: For each study, the following items were abstracted: source of support, pharmacotherapy, site location, treatment setting, patient phase, psychotic episode number, duration, number of men and women in the total sample, mean age of the sample, and the presence of women-specific inclusion/exclusion criteria.

Data Synthesis: Sixty-seven studies published between 1993 and August 2005 met criteria. The median percentage of women in the total sample was 33.3%, the minimum was 6.7% and maximum was 71.2%. A stepwise linear regression analysis showed that age (younger samples), center location (US and Canada), treatment patient setting (inpatient) and ziprasidone trials were all associated with relatively lower percentages of women.

Conclusion: Sex differences in antipsychotic pharmacokinetic and pharmacodynamic that may result in differential effectiveness and susceptibility to adverse effects cannot be ascertained when the percentage of women in clinical trials is as low as it is. Increasing efforts should be made to include more women in new antipsychotic trials in order to accurately determine optimal dosing and guidelines for women patients.

References:

1. Seeman MV. Gender differences in the prescribing of antipsychotic drugs. Am J Psychiatry. 2004;16:1324-33.
2. Gandhi M, Aweeka F, Greenblatt RM, Blaschke TF. Sex differences in pharmacokinetics and pharmacodynamics. Annu Rev Pharmacol Toxicol. 2004;44:499-523.

NR329 Tuesday, May 23, 12:00 PM - 2:00 PM

Length of Stay of Psychiatric Patient and Its Correlate in Mental Health-related Facilities

Seong-Jin Cho, M.D. *Incheon*, Byoung Jo Lee, M.D., Yong-Ik Kim, Ph.D., Jin-Pyo Hong, M.D., Dong-Woo Lee, M.D., Maeng Je Cho, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to know contributing factors that influence the length of stay in mental health related facilities in republic of korea, and to recognize that evaluation of appropriateness is needed for admission to mental health facility

Summary:

Object: This study was aimed to find the contributing factors that influence the length of stay in mental health related facilities and to present future direction for the mental health policy.

Methods: The 1,875 patients who are aged between eighteen and sixty-five are chosen by the stratified random sampling from ten psychiatric hospitals, six psychiatric nursing facilities and five homeless asylums. We investigate about length of stay of all subjects by sociodemographic characteristics, socioeconomic status, functional status, disease related characteristics and analyse contributing factors.

Results: From total subjects, average length of stay was 1,906 days, and facilities, where subjects are institutionalized, explains 40% of length of stay. Other related factors are female, old age, single, lack of supportive system before admission and after discharge, medical assistance type I, unavailable of public transportation and utility, long duration of illness, and psychotic disorder.

Conclusion: For lowering the rate of long-term hospitalization, evaluation of appropriateness is needed for admission to nursing facility and homeless asylum and make up for the medical payment system and the supportive system from family and community.

References:

1. Citrome L et al.:Length of stay and recidivism on a psychiatric intensive care unit.Hosp Commun Psychiatry 1994; 45:74-76.
2. Stoskopf C et al.: Predicting length of stay for patients with psychoses. Health Serv REs 1992; 26:743-766.

NR330 Tuesday, May 23, 12:00 PM - 2:00 PM

Efficacy of Ziprasidone Against Hostility in Schizophrenia

Leslie L. Citrome, M.D. *Nathan S Kline Institute for Psychiatric Research, 140 Old Orangeburg Road, Building 37, Orangeburg, NY, 10962*, Jan Volavka, M.D., Pal Czobor, Ph.D., Shlomo Brook, M.D., Antony D. Loebel, M.D., Francine Mandel, Ph.D.

Educational Objectives:

The participant should be able to recognize that ziprasidone can be used to treat patients with schizophrenia who exhibit hostility, and that ziprasidone is more effective than haloperidol in this regard.

Summary:

Objective: To determine the effects of ziprasidone on hostility.

Method: 572 patients diagnosed with schizophrenia or schizoaffective disorder were the subjects in a randomized, rater-blinded, 6-week open-label study comparing sequential intramuscular and oral ziprasidone with haloperidol. The Brief Psychiatric Rating Scale (BPRS) was the principal outcome measure. To determine the effect of ziprasidone on hostility, post-hoc analyses of the "hostility" item from the BPRS were conducted. Introducing positive symptoms and akathisia as covariates tested specific anti-hostility effect. The effect size for change in hostility status over time was estimated using the odds ratios (OR) computed from generalized estimating equations. The analysis comparing ziprasidone with haloperidol was set up so that the OR indicates the likelihood (odds) of shifting 1 point down on the hostility item in the ziprasidone group compared to the haloperidol group (thus an OR>1 would indicate superiority for ziprasidone).

Results: Without accounting for covariates, both the ziprasidone group and the haloperidol group improved with respect to hostility over time. However, ziprasidone was superior to haloperidol in the likelihood of reduction of hostility, as noted by OR > 1 for the effect of treatment and time. Statistical significant differences are maintained up until Day 42, at which point the differences reached trend levels (p=0.0557). When the following covariates were added, BPRS positive symptoms (suspiciousness, grandiosity, unusual thought content, conceptual disorganization, and hallucinatory behavior), and akathisia, only the ziprasidone group demonstrated a statistically significant improvement over time. The OR favoring ziprasidone over haloperidol remained > 1, and remained statistically significant up to and including Day 7.

Conclusion: Ziprasidone demonstrated specific anti-hostility effects over time throughout the 42-day study period, and statistically significant superiority to haloperidol on this measure in the first week of treatment. Ziprasidone is an effective treatment for hostility in patients with schizophrenia or schizoaffective disorder.

References:

1. Citrome L et al: Science-based treatment of aggression and agitation. In Science, Treatment, and Prevention of Antisocial Behaviors: Evidence-Based Practice, Vol 2, edited by Fishbein D, Kingston, NJ, Civic Research Inst., 2004, pp11.1-11.31.
2. Citrome L, Volavka J, Czobor P, et al: Effects of clozapine, olanzapine, risperidone, and haloperidol on hostility in treatment-resistant patients with schizophrenia and schizoaffective disorder. Psychiatr Serv 2001;52:1510-1514.

NR331 Tuesday, May 23, 12:00 PM - 2:00 PM

Benefits of a Second Dose of Intramuscular (IM) Aripiprazole to Control Agitation in Patients With Schizophrenia or Bipolar I Disorder

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to appreciate that treatment of agitation in patients diagnosed with acute schizophrenia or bipolar I disorder can require multiple injections. They should be aware that a second intramuscular injection of aripiprazole or haloperidol reduces symptoms in agitated patients who do not initially respond, as shown by an analysis of efficacy data from a placebo-controlled trial of patients with schizophrenia. They also should be aware that a second intramuscular injection of aripiprazole or lorazepam reduces symptoms in agitated patients with bipolar I disorder who do not initially respond, as demonstrated by an analysis of efficacy data from a placebo-controlled trial.

Summary:

Objective: To assess the efficacy of intramuscular aripiprazole versus placebo in patients with schizophrenia or bipolar I disorder who require a second intramuscular injection to control agitation. **Methods:** Agitation was defined as having a baseline PANSS Excited Component (PEC) score of 15-32. In the schizophrenia study, 448 agitated patients (age 18-69 years) were randomized to receive injections of aripiprazole (10mg), haloperidol (6.5mg), or placebo. In the bipolar I disorder study, 301 agitated patients (age 18-79 years) were randomized to receive injections of aripiprazole (10mg or 15mg), lorazepam (2mg), or placebo. Patients received ≤3 injections within 24 hours. PEC and Clinical Global Impression-Improvement [CGI-I] scores were assessed in all patients for whom a second injection was deemed appropriate. Mean change from baseline comparisons were analyzed using an ANCOVA model controlling for treatment and baseline value. **Results:** The percentage of patients receiving a second injection for the schizophrenia trial were: aripiprazole, 41%; haloperidol, 34%; placebo, 57%, and for the bipolar disorder trial were: aripiprazole, 35%; lorazepam, 35%; placebo, 64%. In the schizophrenia study, mean changes in PEC scores from pre-second injection to 2 hours post-second injection were significantly reduced by aripiprazole 10mg (-5.9) versus placebo (-2.2, $P \leq 0.01$). In the bipolar disorder study, mean changes in PEC scores were significantly reduced by aripiprazole 10mg or 15mg (-7.7 and -6.0, respectively) versus placebo (-3.1, $P \leq 0.05$). In the schizophrenia study, mean CGI-I scores were significantly improved for aripiprazole 10mg versus placebo ($P \leq 0.01$). In the bipolar disorder study, mean CGI-I scores were significantly improved for aripiprazole 10mg or 15mg versus placebo ($P \leq 0.05$). Both haloperidol 6.5mg and lorazepam 2mg significantly reduced PEC scores and improved CGI-I in all studies ($P \leq 0.01$). **Conclusions:** Aripiprazole efficaciously reduced agitation and improved overall outcome in patients with schizophrenia or bipolar I disorder requiring a second injection.

References:

1. Oren D, Iwamoto T, Marcus R, et al: Intramuscular Aripiprazole vs Placebo for Agitation in Acute Mania. Presented at: Annual Meeting American Psychiatric Association, Atlanta, GA, USA, May 21-26, 2005.
2. Yocca F, Marcus R, Oren D, et al: Intramuscular Aripiprazole in Acute Schizophrenia: A Pivotal Phase III Study. Annual Meeting of the American Psychiatric Association, Atlanta, GA, USA, May 21-26, 2005.

NR332 Tuesday, May 23, 12:00 PM - 2:00 PM

Validity of Proposed Criteria for Evaluating Symptomatic Remission in Schizophrenia

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Educational Objectives:

After this poster presentation, the reader will have learnt about the feasibility and validity of using the "Remission in Schizophrenia Working Group", proposed criteria derived from SANS y SAPS scales as tools for use in everyday clinical practice to assess the symptomatic remission in patients with schizophrenia.

Summary:

Objective: To validate the short forms of the SAPS and SANS proposed by "The Remission in Schizophrenia Working Group" for assessing symptomatic remission in patients with schizophrenia in clinical practice. **Methods:** Reliability of the the sf-SAPS (4 items) and the sf-SANS (5 items) and their convergent validity with the Global Clinical Impression (GCI) and the EQ-5D visual analog scale (VAS) were examined using data from 445 patients with schizophrenia included in two clinical studies in Spain, in which the standard SANS and SAPS were administered. **Results:** The area under the ROC curve and the r^2 with the standard forms were satisfactory (0.92 and 0.82 for SAPS; 0.94 and 0.91 for SANS). Cronbach's alpha was 0.90 for the total score, 0,80 for the sf-SAPS and 0.91 for the sf-SANS. Statistically significant ($p<0.01$) correlations with the EQ-5D VAS and GCI were observed for all items in the reduced scales. ANOVA for lineal trend between each item and the GCI and the EQ-5D VAS showed statistically significant results ($p<0.001$). **Conclusions:** The proposed SAPS and SANS short forms explain most of the variance of the longer forms, show good reliability and validity, and are a candidate tool to assess symptomatic remission in with patients schizophrenia in clinical practice.

References:

1. Andreasen NC, Carpenter WT, Kane JM, Lasser RA, Marder SR, Weinberger DR. Remission in Schizophrenia: Proposed Criteria and Rationale for consensus. Am J Psychiatry 2005; 162:441-449.
2. Andreasen NC, Olsen S. Negative v positive schizophrenia: definition and validation. Arch Gen Psychiatry 1982; 39:789-794.

NR333 Tuesday, May 23, 12:00 PM - 2:00 PM

Metaboloic Disturbance in Clozapine Treated Patients

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Educational Objectives:

Appreciation of metabolic risks in patients undergoing treatment with clozapine

Summary:

Introduction

Patients on clozapine may be particularly susceptible to metabolic disturbance and rates of type-2 diabetes as high as 37% have been reported with longer-term treatment (1). Our goal was to determine the rate of type-2 diabetes as well as pre-diabetic metabolic disturbance (as reflected by rates of the metabolic syndrome and fasting insulin levels) in patients on long-term clozapine therapy.

Methods

Clozapine patients (n=119) were screened with a fasting glucose, insulin, lipid profile, waist circumference and blood pressure. Rates of diabetes (fasting glucose), the metabolic syndrome (ATP 3 criteria) and fasting insulin levels were compared with healthy volunteers screened in the same manner.

Results

Eleven percent (10% males; 13% females) of the patients had diabetes (age 47±8 yr, 80% Caucasian, 60% male, 60% outpatients, and 65 ± 37 mth clozapine treatment). Non diabetic patients had markedly elevated rates of the metabolic syndrome 51% (46% male; 57% female) and fasting insulin 58 ± 40 pmol/L (males55 ± 44 ; females 62 ± 32) relative to the healthy controls.

Conclusions

While rates of diabetes appear to be lower than previously reported, clozapine treated patients have very high rates of the metabolic syndrome and hyperinsulinemia and should be targeted for intervention strategies to reduce coronary heart disease risk and prevent progression to diabetes.

References

References:

1. 1.Henderson DC, Cagliero E, Gray C, Nasrallah RA, Hayden DL, Schoenfeld DA, Goff DC: Clozapine, diabetes mellitus, weight gain, and lipid abnormalities: A five-year naturalistic study. Am J Psychiatry 2000; 157(6):975-81.
2. Kivircik BB, Alptekin K, Caliskan S, Comlekci A, Oruk G, Tumuklu M, Kurklu K, Arkar H, Turk A, Caliskan M, Yesil S: Effect of clozapine on serum leptin, insulin levels, and body weight and composition in patients with schizophrenia. Prog Neuropsychop.

NR334 Tuesday, May 23, 12:00 PM - 2:00 PM

Changes in Weight and Weight-Related Quality of Life in Aripiprazole Versus Standard-of-Care Treatment

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Educational Objectives:

At the conclusion of the presentation, the participant should be able to demonstrate increased knowledge about the measurement of weight-related quality of life and real life impact of weight on weight-related quality of life in patients with schizophrenia.

Summary:

Background: Weight gain is a distressing side effect of antipsychotic medications in patients with schizophrenia[1]. This naturalistic trial investigated mean changes in weight and weight-related quality of life in community-treated patients with schizophrenia.

Methods: Weight and weight-related QOL were assessed at baseline and weeks 8, 18, and 26 in patients with schizophrenia (n = 555) participating in a randomized open-label study comparing aripiprazole treatment to standard-of-care. Weight-related quality of life was assessed with the Impact of Weight on Quality of Life-Lite (IWQOL-Lite) questionnaire, a 31-item instrument that provides a total score and five domain scores (Physical Function, Self-Esteem, Sexual Life, Public Distress, and Work.) [2]. Adjusted mean changes from baseline was compared between groups using ANOVA.

Results: Baseline characteristics were comparable between groups. Significant differences ($p<0.001$) were found in mean weight change, with aripiprazole decreasing -1.3 kg and standard-of-care increasing 1.4 kg by end of study. Significant improvements in quality of life were observed in aripiprazole relative to standard-of-care at weeks 8, 18 and 26 for Physical Function ($p = 0.048$; $p = 0.007$; $p = 0.004$) and Self-Esteem ($p = 0.007$; $p < 0.001$; $p < 0.001$), and at weeks 18 and 26 for Sexual Life ($p = 0.007$; $p = 0.031$), and Total Score ($p < 0.001$; $p = 0.001$). No differences were observed between groups on the Public Distress or Work domains at any assessment.

Conclusions: Compared to standard-of-care, patients with schizophrenia treated with aripiprazole experienced decreased weight and improved weight-related quality of life over 26-weeks, demonstrating that significant quality of life improvements are achieved in a brief time frame.

References:

1. Kolotkin, RL, Crosby, RD, Corey-Lisle, PK, Li, H,. Swanson, JS: Performance of a Weight-Related Measure of Quality of Life in a Psychiatric Sample. Quality of Life Research, in press.
2. Kolotkin RL, Crosby RD, Kosloski KD, Williams GR: Development of a brief measure to assess quality of life in obesity. Obes Res 2001;9: 102-111.

NR335 Tuesday, May 23, 12:00 PM - 2:00 PM

Intramuscular (IM) Aripiprazole Controls Agitation in Patients With Schizophrenia or Bipolar Disorder Without Excessive Sedation

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to list sedation as a common side effect of many medications used to treat agitation in schizophrenia or bipolar I disorder. They should be aware that intramuscular injection of aripiprazole or haloperidol effectively reduces symptoms of agitation without causing overt sedation, as demonstrated by a pooled analysis of efficacy data from two placebo-controlled trials of patients with schizophrenia. They should also be aware that intramuscular injection of aripiprazole or lorazepam significantly reduces symptoms of agitation in patients with bipolar I disorder without causing overt sedation, as demonstrated by an analysis of efficacy data from a placebo-controlled trial.

Summary:

Objective: Demonstrate that IM aripiprazole improves agitation without excessive sedation in patients with schizophrenia (placebo-controlled trials S1 and S2) or bipolar I disorder (placebo-controlled trial BP1).

Methods: Efficacy data were obtained from trials S1 (N = 445) and S2 (N = 232) of IM aripiprazole (10 or 15 mg) and haloperidol (6.5 or 7.5 mg), and trial BP1 (N = 291) of IM aripiprazole (10 or 15 mg) and lorazepam 2 mg. PANSS Excited Component (PEC) and Agitation-Calmness Evaluation Scale (ACES) scores were

assessed 1 hour prior and 2 hours following the first injection. Excessive sedation was defined as an ACES score ≥8.

Results: In trials S1 and S2, 94.1% of aripiprazole-treated and 92.1% of haloperidol-treated patients were not considered excessively sedated 2 hours after injection. In trial BP1, 92.0% of aripiprazole-treated and 85.3% of lorazepam-treated patients were not considered excessively sedated. Across all studies, 97.3% of placebo-treated patients were not considered excessively sedated. In patients without excessive sedation in trials S1 and S2, aripiprazole (10 mg and 15 mg) and haloperidol (6.5 mg and 7.5 mg) significantly reduced PEC scores compared with placebo ($P < 0.005$). In patients without excessive sedation in trial BP1, aripiprazole (10 mg and 15 mg) and lorazepam (2 mg) significantly reduced PEC scores compared with placebo ($P < 0.005$).

Conclusions: IM aripiprazole effectively reduced agitation in patients with schizophrenia or bipolar I disorder, independent of excessive sedation.

References:

1. Daniel D, Stock E, Wilber R, et al: Intramuscular Aripiprazole in Acutely Agitated Psychotic Patients. Presented at: Annual Meeting of the American Psychiatric Association, New York, NY, USA, May 1-6, 2004.
2. Yocca F, Marcus R, Oren D, et al: Intramuscular Aripiprazole in Acute Schizophrenia: A Pivotal Phase III Study. Presented at: Annual Meeting of the American Psychiatric Association, Atlanta, GA, USA, May 21-26, 2005.

NR336 Tuesday, May 23, 12:00 PM - 2:00 PM

Transitioning From Intramuscular (IM) to Oral Aripiprazole in Patients With Schizophrenia

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to appreciate the importance of transitioning from intramuscular to oral antipsychotics in the long-term treatment of patients with schizophrenia. They should also be aware that analysis of efficacy data from a placebo-controlled trial demonstrated that safety and efficacy during the transition from intramuscular to oral aripiprazole is comparable to that of haloperidol.

Summary:

Objective: Assess the effectiveness and safety of transitioning patients with acute schizophrenia from IM to oral aripiprazole.

Methods: A total of 360 agitated patients (18-69 years) were randomized to receive ≤3 IM injections of aripiprazole 10 mg or haloperidol 6.5 mg within 24 hours. Inclusion criteria were PANSS Excited Component (PEC) total scores between 15-32 and ≥4 on at least 2 PEC items. Patients (n = 304) were then transitioned to oral formulations (aripiprazole 10-15 mg/d or haloperidol 7-10 mg/d) for 4 days. Patients were assessed using PEC, Clinical Global Impression-Improvement (CGI-I), and Clinical Global Impression-Severity of Illness (CGI-S) Scale scores, as well as the Agitation Calmness Evaluation Scale (ACES), and the Corrigan Agitated Behavior Scale (CABS). Mean changes from baseline (last value obtained during IM treatment) to endpoint (Day 5, LOCF) were analyzed using an ANCOVA model controlling for treatment, country, and baseline value.

Results: PEC scores were reduced 24 hours after IM injection with either aripiprazole or haloperidol (mean change of -8.3 and -8.1, respectively). Improvements in all other scales were also observed 24 hours following IM injection of aripiprazole or haloperidol. Treatment with oral aripiprazole or haloperidol for 4 days further reduced mean PEC scores (-1.4 for both aripiprazole and haloperidol). Reductions in all other scales were also maintained for 4 days following the transition to oral therapies. The incidence of AEs, and changes in laboratory values and vital signs were similar for both phases.

Conclusions: The effectiveness of aripiprazole and haloperidol appears to be maintained in patients with schizophrenia following transition from IM to oral formulations.

References:

1. Wright P, Meehan K, Birkett M, et al: A comparison of the efficacy and safety of olanzapine versus haloperidol during transition from intramuscular to oral therapy. Clin Ther 2003; 25:1420-1428.
2. Yocca F, Marcus R, Oren D, et al: Intramuscular Aripiprazole in Acute Schizophrenia: A Pivotal Phase III Study. Presented at: Annual Meeting of the American Psychiatric Association, Atlanta, GA, USA, May 21-26, 2005.

NR337 Tuesday, May 23, 12:00 PM - 2:00 PM

Switch from atypical APs to long-acting risperidone: symptom control in French patients

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Educational Objectives:

After reading this poster the participant will understand how to evaluate the improvements in symptom control seen in patients with schizophrenia treated with a long-acting injectable atypical antipsychotic.

Summary:

Objective: To investigate the effects on symptom control and functioning of a direct transition from oral atypical antipsychotics to risperidone long-acting injectable (RLAI) in patients with schizophrenia or other psychotic disorders requiring a change of treatment.

Methods: Adults with schizophrenia or other psychotic disorders who were clinically stable for ≥1 month, but required a change in their medication, received RLAI 25 mg (increased to 37.5 mg or 50 mg, if necessary) every 2 weeks for 6 months.

Results: A subgroup analysis was performed with130 French patients (69% male, mean age 36±12 years). The majority of these patients (84%) suffered from DSM-IV schizophrenia (mainly paranoid). At endpoint, 41% of patients showed an improvement ≥20% in PANSS total score. Mean total PANSS score was reduced from baseline to endpoint (78.3 versus 67.8; $p<0.001$). Significant improvements were also seen in all three PANSS subscales and in almost all symptom factors. There were significant improvements ($p<0.001$) from baseline to endpoint in mean scores for CGI-Disease Severity (4.4 versus 3.6) and GAF (53.2 versus 59.8).

Conclusion: Transition from an oral atypical antipsychotic to RLAI resulted in significant improvements in symptom control and functioning in patients in France.

References:

1. Lindenmayer JP, et al. Safety and efficacy of long-acting risperidone in schizophrenia A 12-week, multicenter, open-label study in stable patients switched from typical and atypical oral antipsychotics. J Clin Psychiatry 2004; 65: 1084-1089.
2. Moeller H, Llorca P, Sacchetti E, Martin S, Medori R, Parellada E. Efficacy and safety of direct transition to risperidone long-acting injectable in patients treated with various antipsychotic therapies. Int Clin Psychopharmacol 2005;20(3):121-130.

NR338 Tuesday, May 23, 12:00 PM - 2:00 PM

Efficacy, Safety and Effect on Functioning of Oral Paliperidone Extended-Release Tablets in the Treatment of Acute Schizophrenia: an International 6-Week Placebo-Controlled Study

Michael Davidson, M.D. *Tel Aviv University, Department of Psychiatry, Tel Aviv Einstein street, Tel Aviv, 69978, Israel*, Robin Emsley, M.D., Michelle Kramer, M.D., Cristiana Gassmann-Mayer, Ph.D., Pilar Lim, Ph.D., James Pan, Ph.D., Marielle Eerdekens, M.D.

Educational Objectives:

At the conclusion of this presentation, participants should be able to describe the efficacy and tolerability of the investigational drug paliperidone extended-release, and the effect on functioning during the treatment of acute schizophrenia as assessed using the Personal and Social Performance scale.

Summary:

Objective-This study assessed efficacy, safety and effect on functioning of investigational paliperidone extended-release (paliperidone Extended Release) tablets in patients with acute schizophrenia.

Method-This double-blind, parallel-group, dose-response study randomized patients (n=618; age ≥18 years) to receive paliperidone Extended Release 3mg, 9mg, or 15mg, placebo or olanzapine 10mg daily. Olanzapine 10mg was included for assay sensitivity only and the study powered to assess efficacy of paliperidone Extended Release versus placebo.

Results-Baseline mean PANSS total score in the intention-to-treat group (n=605) was 93.0±12.5 (similar between groups) and the mean age=36.8y. Mean PANSS total score at endpoint improved for paliperidone Extended Release versus placebo (3mg=-15.0±19.6, 9mg=-16.3±21.8, 15mg=-19.9±18.4, placebo=-2.8±20.9; p<0.001 [olanzapine change=-18.1±20.3]). Improvement from ≥Day 4 (first observation point) was demonstrated for paliperidone Extended Release versus placebo (p<0.05). Personal and Social Performance Scale scores improved at endpoint for paliperidone Extended Release versus placebo (3mg= 8.3±17.1, 9mg=7.6±14.2, 12mg=12.2±15.7, placebo=-1.5±15.8; p<0.001). Treatment-emergent adverse event-EPS were comparable for paliperidone Extended Release 3mg, olanzapine and placebo, although higher with paliperidone Extended Release 9mg and 15mg. Serious adverse event frequency was similar between paliperidone Extended Release (7%), olanzapine (6%) and placebo (7%).

Conclusions-In this study, treatment with paliperidone Extended Release 3mg, 9mg and 15mg was well tolerated and effective and associated with functional improvements in patients with schizophrenia.

References:

1. Falkai P, Wobrock T, Lieberman J, et al.: World Federation of Societies of Biological Psychiatry (WFSBP) guidelines for biological treatment of schizophrenia, Part 1: acute treatment of schizophrenia. World J Biol Psychiatry 2005; 6(3):132-191.

2. Practice guidelines for the treatment of patients with schizophrenia (2nd Edition), February 2004. Available at: http://www.psych.org/psych_pract/treatg/pg/Practice20Guidelines8904/Schizophrenia_2e.pdf.

NR339 Tuesday, May 23, 12:00 PM - 2:00 PM

Evaluation of the Metabolic Safety of Aripiprazole

Marc De Hert, M.Eng. *UC St. Jozef, Leuvensesteenweg 517, Kortenberg, B 3070, Belgium*, Linda Hanssens, M.S., Dominique Van Eyck, M.D., Martine Wampers, Psy.D., Andre Scheen, Prof. Dr., Jozef Peuskens, Prof. Dr.

Educational Objectives:

At the conclusion of the presentation the participant should have an understanding of the specific metabolic properties of a novel antipsychotic, aripiprazole.

Summary:

Background: Metabolic abnormalities are frequent in patients treated with antipsychotics, and are a growing concern to clinicians.

Method: The metabolic safety of aripiprazole was evaluated in a projective study. All patients underwent an extensive metabolic evaluation, including an oral glucose tolerance test (OGTT), at baseline, at 6 weeks and at 3 months follow-up. 25 schizophrenic patients were included in the study. 5 patients met criteria for diabetes on their previous antipsychotic treatment at the moment of switch to aripiprazole.

Results: At 3 months follow-up there was a significant reduction in weight and waist circumference. There was a significant reduction in fasting glucose, fasting insulin, insulin resistance and serum lipids (cholesterol, triglycerides, LDH and non-HDL cholesterol).

There was also a significant reduction of prolactine.

All cases of recent onset diabetes were reversible at 3 months follow-up. Four patients had normal glucose values fasting and at 120 min in the OGTT. One patient had impaired glucose tolerance at endpoint.

At baseline 57.1% of patients switched to aripiprazole met criteria for ATP-III metabolic syndrome. At endpoint their was a significant reduction in the prevalence of ATP-III metabolic syndrome (9.5%, p=0.0011).

Conclusion: Our prospective data confirm the metabolic safety of aripiprazole. Our results support the reversibility of recent onset diabetes on antipsychotic medication, if detected early and when switch is done to a safer metabolic antipsychotic.

Acknowledgement: Educational grant from global epidemilogy and outcomes research (GEOR) BMS

NR340 Tuesday, May 23, 12:00 PM - 2:00 PM

The Metabolic Syndrome in Patients With Schizphrenia

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Educational Objectives:

At the conclusion of the presentation the participant will know the current definitions of the metabolic syndrome and will be able to understand why screening for the metabolic syndrome in patients with schizophrenia is important.

Summary:

Background: The presence of the metabolic syndrome is an important risk factor for cardiovascular disease and diabetes. There are limited data on the prevalence of the metabolic syndrome in European patients suffering from schizophrenia.

Methods: All consecutive patients with schizophrenia at our university psychiatric hospital and affiliate services were entered in an extensive prospective metabolic study including an oral glucose tolerance test. The prevalence of the metabolic syndrome was assessed based on the National Cholesterol Education Program criteria (NCEP, Adult Treatment Protocol, ATP III), adapted ATP-III criteria using a fasting glucose threshold of 100mg/dl (AHA) and on the recently proposed criteria from the International Diabetes Federation (IDF).

Results: The analysis of 430 patients showed a prevalence of the metabolic syndrome of 28.4% (ATP-III), 32.3% (ATP-III A) and 36% (IDF), respectively. The prevalence of the metabolic syndrome in our sample of patients with schizophrenia is at least twice as high compared to an age-adjusted community sample in Belgium.

Conclusion: The metabolic syndrome is highly prevalent among treated patients with schizophrenia. It represents an important risk for cardiovascular and metabolic disorders. Assessment of the presence and monitoring of the associated risks of the metabolic syndrome should be part of the clinical management of patients treated with antipsychotics.

Acknowledgement: Educational grant from global epidemilogy and outcomes research (GEOR) BMS

NR341 Tuesday, May 23, 12:00 PM - 2:00 PM

Comparison of Insight and Neuropsychological Function in Patients With Schizophrenia and Bipolar Disorder in Remission.

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Educational Objectives:

At the conclusion of this presentation, the participant should gain knowledge on the differences in insight in patients with schizophrenia and bipolar disorder in remission. Meaningful associations between insight and neuropsychological function will also be discussed for both patient groups, supporting the notion that insight is a multidimensional construct, possibly with different neurobiological substrates in schizophrenia and bipolar disorder.

Summary:

Objective: Our aim was to investigate insight in patients with schizophrenia and bipolar disorder in remission, and its relationship with neuropsychological function in both disorders, and to clarify whether patients with schizophrenia differ from patients with bipolar disorder.

Methods: We administered the shortened version of the Scale to Assess Unawareness of Mental Disorder (SUMD) and a neuropsychological test battery to a sample of 41 patients in remission (20 with schizophrenia and 21 with bipolar disorder).

Results: Patients with schizophrenia scored significantly higher in the SUMD, indicating that their level of insight was significantly lower than in bipolar patients.

A negative correlation was found between age of disease onset and level of insight in patients with schizophrenia. No correlation was found between reduced insight and age, educational level, disease duration, number of admissions, and overall functioning for both patient's groups. A positive correlation was found between overall awareness and awareness for a mental disorder, and Digit Span scores in bipolar patients. Bipolar patients with better scores on Trail-Making Test (Part A) and on Symbol Digit Modalities Test had more intact insight for the social consequences of the disease and for the medication effects, respectively.

Conclusions: Patients with schizophrenia showed significantly reduced insight as compared to bipolar patients. Even though there were no significant differences between the groups in the majority of the neuropsychological tests' performance, reduced insight was associated with impaired frontal lobe functioning in the bipolar group only.

References:

1. Yen C-F, Chen C-S, Yeh ML, et al. Comparison of insight in patients with schizophrenia and bipolar disorder in remission. J Nerv Ment Dis 2002; 190(12):847-9.
2. Young DA, Zakzanis KK, Bailey C, et al. Further parameters of insight and neuropsychological deficit in schizophrenia and other chronic mental disease. J Nerv Ment Dis 1998; 186(1):44-50.

NR342 Tuesday, May 23, 12:00 PM - 2:00 PM

Direct Effect of Paliperidone Extended-Release Tablets on Negative Symptoms

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Educational Objectives:

After viewing this presentation, participants should be able to understand the concepts involved in a path analysis, and the direct and indirect effects of paliperidone on negative symptoms in acutely ill patients with schizophrenia.

Summary:

Objective: While all antipsychotic medications have efficacy in the treatment of positive symptoms, not all are directly effective against negative symptoms. Studies have shown that an investigational psychotropic, paliperidone extended-release (paliperidone Extended Release) tablets, significantly reduce negative symptom subscale scores on the Positive and Negative Syndrome Scale (PANSS). While these effects on negative symptoms may result from changes in mood and extrapyramidal symptoms, this report further evaluates the direct effects of paliperidone Extended Release on negative symptom improvement.

Methods: A post-hoc analysis of data from three pooled 6-week, double-blind, placebo-controlled studies of paliperidone Extended Release in patients (n=937) with acute schizophrenia was conducted. Regression analyses identified which baseline/study characteristics affect negative symptoms. Change at endpoint on the PANSS negative factor score was the dependent variable. Independent variables tested include demographic and clinical characteristics. Path analysis determined the extent of direct and indirect effects of paliperidone Extended Release on changes in negative symptoms. Factors identified as indirect modulators of negative symptoms included changes in positive symptoms, depressive symptoms, and movement disorders (Simpson Angus Scale total score).

Results: Significant predictors of change in negative symptom scores were duration of paliperidone Extended Release exposure ($P<0.001$) and change in Personal and Social Performance scale score ($P<0.001$). After correcting for indirect effects, the path analysis model showed that 33% of negative symptom change was a direct effect of paliperidone Extended Release . The indirect effects of paliperidone Extended Release on negative symptoms were modulated through change in positive symptoms (51%) and depressive symptoms (18%). Changes in movement disorders only accounted for a 2.1% inverse effect on negative symptoms.

Conclusions: While negative symptom improvement was indirectly mediated through changes in positive and depressive symptomatology, this analysis supports the hypothesis that there is a direct effect of paliperidone Extended Release on the negative symptoms of schizophrenia in this acutely ill patient population.

Sponsored by Janssen, LP.

References:

1. Tollefson GD, Sanger TM: Negative symptoms: a path analytic approach to a double-blind, placebo- and haloperidol-controlled clinical trial with olanzapine. Am J Psychiatry 1997; 154:466-474.

2. Pedhazur EJ: Multiple regression in behavioral research, 2nd edition. New York, NY, Holt, Rinehart and Winston, 1982, pp. 577-635.

NR343 Tuesday, May 23, 12:00 PM - 2:00 PM

The Acute Management of Agitation in the Pregnant Patient

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to:

1) Discuss the impact of antipsychotic medication and benzodiazepines on pregnant women and the fetus.

2) To discuss management strategies for pregnant women who are treated in a psychiatric emergency service.

Summary:

Objective: To better understand how agitated pregnant women are pharmacologically managed in a psychiatric emergency service (PES).

Method: A retrospective chart review was conducted on 80 women admitted to the Crisis Response Center (CRC) with HCG-positive urine, from January 1, 2004 to June 30, 2005. Data analyzed included demographics (age, ethnicity, housing status, insurance status), admitting complaint, medical status, drug use, and medical management in the CRC, pregnancy awareness, prenatal care, trimester, and pregnancy outcomes. When available, data regarding pregnancy outcomes, such as type of delivery, APGAR scores, weight, and complications was obtained from Temple University Hospital Systems (TUHS) records. Demographic profiling and characterization of other variables was completed using simple frequency calculations and cross tabulations with SPSS.

Results: Thirty-one (39%) of the subjects received psychotropic medication. A total of 34 doses were administered to these subjects; only three patients required a second dose. Eight (24%) of the 34 doses administered were a benzodiazepine, 16 (47%) doses were an antipsychotic only, and 10 (29%) were a combination of a benzodiazepine and an antipsychotic. Haloperidol alone, or in combination with a benzodiazepine, [12 (35%)] was the most frequently administered psychotropic. Three patients only received clonidine, trimethobenzamide, and dicyclomine for opiate withdrawal symptoms. Two patients required brief restraint for assaultive behavior that was unresponsive to any other intervention. Of eleven patients for whom delivery records were available, only two received medication in the PES. All of the women had uneventful deliveries with babies having normal birth weights and APGAR scores.

Conclusion: Acute agitation can successfully be managed with antipsychotics and/or benzodiazepines. Haloperidol, given as a single agent, is the authors' preferred drug. However, the minimal amount of medication necessary should be used and any intervention should also include interpersonal management techniques to attenuate the agitation.

References:

1. Allen MH, Currier GW, Hughes DH: Medication strategies for a pregant woman who is agitated, psychotic, and unresponsive to direction. The Expert Consensus Guideline Series. In: Treatment of Behavioral Emergencies. Postgraduate Medicine 2001: 48.

2. Altshuler LL, Cohen L, Szuba MP, Burt VK, Gitlin M, Mintz J: Pharmacologic management of psychiatric illness during pregnancy: dilemmas and guidelines. Am J Psychiatry 1996; 153; 592-606.

NR344 Tuesday, May 23, 12:00 PM - 2:00 PM

First-line Treatment With Long-Acting Risperidone in Patients With First-Episode Psychosis: Safety and Efficacy Results From a 6-Month Interim Analysis

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Educational Objectives:

At the end of this presentation the reader should be able to describe the efficacy and safety of long-acting risperidone in patients with first-episode psychosis.

Summary:

Objectives: Assess the safety and efficacy of long-acting risperidone (LAR) in first-episode psychosis.

Methods: This pre-specified, 6-month interim analysis of a 24-month, open-label study, was conducted in 18 women and 33 men. After 1 week of risperidone oro-dispersible tablets (1-3mg), participants received 25mg LAR every 2 weeks for 6 weeks with flexible dosing thereafter (LAR 25-50mg). Assessments included PANSS, relapse rate, adverse events (AEs), ESRS and body mass index (BMI).

Results: Mean age=25.3±7.3 years, with diagnosis of schizophreniform disorder (n=23) or schizophrenia (n=28). Forty-three (86%) subjects completed 6 months. Endpoint doses were 25mg (n=30), 37.5mg (n=15) and 50mg (n=5). Total PANSS scores improved from 90.3±13.8 (baseline) to 53.1±14.7 (6 months; $p<0.0001$) and the response rate (≥50% improvement in total PANSS score) was 74%; five patients relapsed. AEs were mainly mild-to-moderate in severity (96%); 58% judged unlikely related (not related, doubtful) to LAR. The most common AE was headache (n=11 [23.9%]). Serious AEs requiring hospitalization occurred in three patients (5.9% [insomnia; depression; aggression]). ESRS scores were low at baseline and did not change significantly throughout the study. BMI at baseline and 6-months was 20.6±4.6 and 24.2±5.0 ($p<0.0001$), respectively.

Conclusions: LAR was associated with robust symptom improvements, with no unexpected tolerability issues, in patients with first-episode psychosis.

References:

1. Emsley R, Oosthuizen P: Evidence-based pharmacotherapy of schizophrenia. Int J Neuropsychopharmacol. 2004; 7(2):219-238.

2. Practice guidelines for the treatment of patients with schizophrenia (2nd Edition), February 2004. Available at: http://www.psych.org/psych_pract/treatg/pg/Practice20Guidelines8904/Schizophrenia_2e.pdf.

NR345 Tuesday, May 23, 12:00 PM - 2:00 PM

Analysis of the Efficacy and Effect on Function of Paliperidone Extended-Release Tablets in the Treatment of Young Adults With Schizophrenia

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Educational Objectives:

At the conclusion of this presentation, participants should be able to describe the efficacy and the effect on functioning, as assessed using the Personal and Social Performance Scale, of the investigational drug paliperidone ER during the treatment of young adults with schizophrenia.

Summary:

Objective: Early identification and treatment is important in first-episode schizophrenia since prolonged periods of untreated psychosis can reduce functioning and lead to suboptimal outcomes[1,2]. This post-hoc analysis assessed the efficacy, safety and effect on patient functioning of investigational paliperidone extended-release (paliperidone Extended Release) tablets in young adults with schizophrenia.

Method: Data from patients aged 18–25 years (n=243) in the pooled intention-to-treat (ITT) population of three similar 6-week, double-blind, parallel-group, placebo-controlled, dose-response trials were included in these analyses. Patients were randomized to receive paliperidone Extended Release 3mg, 6mg, 9mg, 12mg or 15mg, olanzapine 10mg or placebo. Olanzapine was included for assay sensitivity only and the study powered to assess the efficacy of paliperidone Extended Release versus placebo.

Results: The mean age for this group (based on ITT) was 22.5 (SD=2.06). Baseline mean PANSS total score was 95.0±12.2. Mean PANSS total score at endpoint improved for paliperidone Extended Release versus placebo (3mg=-16.4±16.3 [p=0.278], 6mg=-15.8±19.7 [p=0.021], 9mg=-20.4±22.8 [p=0.019], 12mg=-17.3±23.2 [p=0.007], 15mg=-23.2±21.3 [p=0.046], placebo=-4.0±24.5). The Personal and Social Performance scale (PSP) was used to assess patient function and scores improved at endpoint for paliperidone Extended Release versus placebo (3mg= 7.2±13.5 [p=0.939], 6mg=7.0±18.5 [p=0.088], 9mg=10.8±15.7 [p=0.041], 12mg=8.2±12.4 [p=0.03], 15 mg=15.8±18.3 [p= 0.036], placebo=-1.2±13.2). Mean improvement in total PANSS and PSP were -20.4±20.1 and 11.0±12.5, respectively, for the olanzapine group. Treatment-emergent adverse events were 64%, 56%, 78%, 74%, 76% for paliperidone Extended Release 3mg, 6mg, 9mg, 12mg and 15mg, respectively, 70% for placebo and 78% for olanzapine.

Conclusions: This analysis suggests that treatment with paliperidone Extended Release was effective and associated with functional improvements in young adults with schizophrenia.

References:

1. Emsley R, Oosthuizen P: Evidence-based pharmacotherapy of schizophrenia. Int J Neuropsychopharmacol. 2004; 7(2):219-238.
2. Practice guidelines for the treatment of patients with schizophrenia (2nd Edition), February 2004. Available at: http://www.psych.org/psych_pract/treatg/pg/Practice20Guidelines8904/Schizophrenia.

NR346 Tuesday, May 23, 12:00 PM - 2:00 PM

Body Mass Index, Waist Circumference, and Quality of Life in Individuals With Schizophrenia

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognise the importance of routinely incorporating the measurement of waist circumference into research and clinical practice in relation to schizophrenia, weight management, and the metabolic syndrome.

Summary:

Introduction

Body mass index (BMI) is a common assessment and outcome measure related to weight gain in schizophrenia. However, BMI does not recognize fat distribution and the accumulation of fat in and around the abdominal region associated with obesity. Measures of waist circumference may also be the best single indicator of cardiovascular risk factors and a simpler measure for identifying the need for weight management (1). Our goal was to determine the differential relationship between this measure, BMI, and quality of life.

Methods

Individuals with DSM-IV schizophrenia (n = 93) were interviewed to obtain sociodemographic data, complete a Quality of Life questionnaire (the MOS SF-12) and have measurements taken of height, weight (kg), and waist circumference (cm). Body mass index was calculated (kg/m^2). Correlations among variables were examined.

Results

Mental component score (MCS) was not significantly correlated to any of the weight related measures. These measures were inversely correlated (level $p \leq 0.01$) to the SF-12 physical health summary measure (PCS): BMI (-0.30) and waist circumference (-0.47).

Conclusions

Quality of life in schizophrenic patients is related to measures of body weight and as others have found appears to be primarily experienced as a physical problem (2). However, the relationship is strongest using waist circumference as the primary measure. This provides further support for routinely incorporating this measure within research and clinical assessments.

References:

1. Faulkner G, Soundy AA, Lloyd K: Schizophrenia and weight management: a systematic review of interventions to control weight. Acta Psychiatr Scand 2003; 108: 324-32.
2. Strassnig M, Brar JS, Ganguli R: Body mass index and quality of life in community-dwelling patients with schizophrenia. Schizophr Res 2003; 62: 73-6.

NR347 Tuesday, May 23, 12:00 PM - 2:00 PM

The orexin 1 receptor (*HCRTR1*) gene as a susceptibility gene contributing to polydipsia-hyponatremia in schizophrenia

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Educational Objectives:

Rationale: Our previous study suggested that polydipsia in schizophrenia may have genetic component (Shinkai et al, 2003). Orexin plays an important role in feeding and drinking behavior. In the present study, we examined the association between polydipsia-hyponatremia in schizophrenia and functional polymorphisms in the orexin-1 receptor. *Material and Methods*: Our sample includes 312 patients with schizophrenia (DSM-IV) (65 with polydipsia and 247 without polydipsia). Informed consent was a premise for participation, and this study was approved by the Ethics Committee of the University of Occupational and Environmental Health. Genomic DNA was extracted from 10-ml aliquots of EDTA-anticoagulated venous blood following the standard procedures. Genotyping was assessed by the TaqMan allele-specific assay method using ABI PRISM® 7000 (Applied Biosystems) at the Bio-information Research Center, University of Occupational and Environmental Health. Differences in allele and genotype distribution between cases and controls were evaluated using the χ^2 test.

Results: Significant association between the *HCRTR1* Ile408Val polymorphism and polydipsia was found (genotype: χ^2 = 9.85, df = 2, p = 0.007; allele: χ^2 = 8.00, df = 1, p = 0.0047; OR = 0.53; 95%CI = 0.34-0.83). *Conclusion*: Our results suggest that the *HCRTR1* Ile408Val polymorphism may confer susceptibility to polydipsia in schizophrenia.

Summary:

Rationale: The underlying pathophysiology of primary polydipsia in schizophrenia is poorly understood. Our previous study, however, suggested that this condition may have genetic component (Shinkai et al, 2003). Orexins, also called hypocretin, play an important role in feeding and drinking behavior. Administration of orexin in rats induce increased water intake with a longer-lasting effect than angiotensin II, which is also known as a potent dipsogen. In the present study, we examined the association between polydipsia-hyponatremia in schizophrenia and functional polymorphisms in the orexin-1 receptor. *Material and Methods*: Our sample includes 312 patients with schizophrenia (DSM-IV) (65 with polydipsia and 247 without polydipsia). Informed consent was a premise for participation, and this study was approved by the Ethics Committee of the University of Occupational and Environmental Health. Genomic DNA was extracted from 10-ml aliquots of EDTA-anticoagulated venous blood following the standard procedures. Genotyping was assessed by the TaqMan allele-specific assay method using ABI PRISM® 7000 (Applied Biosystems) at the Bio-information Research Center, University of Occupational and Environmental Health. Differences in allele and genotype distribution between cases and controls were evaluated using the χ^2 test. *Results*: Significant association between the *HCRTR1* Ile408Val polymorphism and polydipsia was found (genotype: χ^2 = 9.85, df = 2, p = 0.007; allele: χ^2 = 8.00, df = 1, p = 0.0047; OR = 0.53; 95%CI = 0.34-0.83). *Conclusion*: Our results suggest that the *HCRTR1* Ile408Val polymorphism may confer susceptibility to polydipsia in schizophrenia.

References:

1. Shinkai et al, 2003.
2. Meerabux et al, 2005.

NR348 Tuesday, May 23, 12:00 PM - 2:00 PM

Reliability, Validity and Sensitivity to Change of the Personal and Social Performance Scale in Patients With Stable Schizophrenia

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Educational Objectives:

At the conclusion of this presentation, participants should understand that the Personal and Social Performance scale is a reliable and valid measure of personal and social function in patients with stable schizophrenia with good construct validity and sensitivity to clinical change.

Summary:

Background: The Personal and Social Performance scale (PSP) as a measure of personal and social functioning has been shown to have good reliability and validity in patients with stabilized schizophrenia[1]. The PSP provides a single composite rating that considers 4 domains of personal and social functioning (socially useful activities, relationships, self-care, aggressive behaviors) over a recall period of 1 month. The objective of this study was to assess the reliability, validity, responsiveness and minimally important difference (MID) of the PSP in an outpatient population with stablized schizophrenia.

Method: Data from two clinical antipsychotic studies (n=411; mean baseline PANSS=66.4 and CGI-S=3.5) were analyzed. Outcome measures included PANSS, CGI-S, Strauss-Carpenter Level of Function (LOF) and PSP. Test-retest reliability for the PSP were assessed and intraclass correlation coefficients (ICC) derived. Convergent and discriminant validity was assessed. Sensitivity of the PSP to clinical change and the MID were evaluated.

Results: The test-retest ICC exceeded 0.70 indicating that the PSP is a reliable scale. The PSP was more highly correlated with LOF (ρ=0.61) than with the PANSS (ρ=-0.45). The PSP was able to discriminate between different levels of CGI severity (p<0.0001). Regression analyses showed that the PSP is sensitive to change in PANSS total score (p<0.0001). Based on a 1 category improvement in CGI-S, the observed between-group MID for PSP in stable patients was 6 to 7 points.

Conclusions: These data support the PSP as a reliable clinician-reported measure of personal and social function in outpatients with stabilized schizophrenia with good construct validity and sensitivity to clinical change.

References:

1. Morosini PL et al.: Development, reliability and acceptability of a new version of the DSM-IV Social and Occupational Functioning Assessment Scale (SOFAS) to assess routine social functioning. Acta Psychiatr Scand 2000; 101(4):323-329.
2. Mueser KT, Tarrier N: Handbook of Social Functioning in Schizophrenia. Boston, Allyn and Bacon, 1998.

NR349 Tuesday, May 23, 12:00 PM - 2:00 PM

A Novel Class of Antipsychotic With Significant Side Effects Reduction

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognise the importance of development a new class of antipsychotics that will significantly reduced side effects, and to understand that BL-1020 has that potential.

Summary:

The current treatment of schizophrenia relies on two classes of drugs. The "typical" antipsychotic, in use 40 years, and effective but have adverse effects (extrapyramidal symptoms- EPS). The newer "atypical" antipsychotics have fewer motor side-effects but have been associated with increased risk of diabetes, and dyslipidemia. The CATIE (Clinical Antipsychotic Trials of Intervention Efficacy) study of drugs to treat schizophrenia, found that older (typical) antipsychotics such as Perphenazine worked just as well as newer (atypical) antipsychotics, although both are limited by their side effect profile.

BL-1020 is a conjugate of the typical antipsychotic Perphenazine and Gamma-aminobutyric acid (Gamma-aminobutyric acid), a naturally accruing inhibitory amino acid. It is designed to target simultaneously the overactivity of dopamine and the hypoactivity of Gamma-aminobutyric acid that have been implicated in schizophrenia. In addition, it targets the Gamma-aminobutyric acid deficiency that may be relevant to antipsychotic-induced EPS. Pharmacokinetic studies demonstrate that BL-1020 provides effective transport of Gamma-aminobutyric acid into the brain, a therapeutic approach that has been challenging due to the inability of exogenously administered Gamma-aminobutyric acid to cross the blood-brain barrier (BBB). In animal models of schizophrenia, single and repeated oral administration of BL-1020 shows significant antipsychotic efficacy with minimal induction of EPS. BL-1020

presents a promising first-in-class molecule, targeting the dopamine and Gamma-aminobutyric acid pathways for the treatment of schizophrenia with a significant reduction in EPS side effects associated with typical antipsychotics and with the potential to be devoid of metabolic adverse effects associated with atypical antipsychotics.

References:

1. Wassef A, Baker J, Kochan LD. GABA and Schizophrenia: A Review of Basic Science and Clinical Studies. J of Clin Psycopharmacology 2003; 23:601-640.

2. Lieberman J.A et al. Effectiveness of anti-psychotic Drugs in patients with chronic schizophrenia. N Engl J Med 2005; 353;1209-1223.

NR350 Tuesday, May 23, 12:00 PM - 2:00 PM

Insight in Schizophrenia: Results From a 12-Month, Double-Blind Study

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Educational Objectives:

At the conclusion of this presentation, the participant will understand the role of insight in patients with schizophrenia and recognize the relationship between insight and its correlates of treatment duration, cognition, and social functioning.

Summary:

Objective: Patients with schizophrenia have poor insight into their illness. This lack of awareness reaches its peak during acute episodes and persists in approximately half of patients throughout their illness. Prior findings suggest insight is associated with improvement of positive, negative, and affective symptoms. We explored the relationship between insight, symptoms, duration of treatment, cognition, and social functioning in a 1-year study of patients with schizophrenia or schizoaffective disorder.

Methods: Stable patients received 25 or 50 mg of long-acting, injectable risperidone every 2 weeks for 1 year. The Positive and Negative Syndrome Scale (PANSS) item G12 (1 = no impairment, 7 = severe impairment) measured insight. Other measures included PANSS negative symptoms factor, Clinical Global Impression of Severity (CGI-S), Strauss-Carpenter Levels of Functioning (LOF), Personal and Social Performance (PSP), and a cognitive test battery. Correlation/regression post-hoc analyses examined associations between insight, treatment duration, and clinical/functional measures.

Results: Baseline insight correlated significantly ($P<0.001$) with baseline CGI-S (r = 0.30), PANSS subscales (range: r = 0.57-0.24), and functioning scores (LOF, r = -0.26; PSP, r = -0.22). There was significant correlation between insight and attention (r = -0.30; $P<0.001$) and declarative memory (r = -0.22, $P<0.001$); and weaker correlations with visual motor (r = -0.13; $P = 0.03$) and social cognition (r = -0.13; $P = 0.04$). Regression models identified significant predictors ($P <0.001$) of PSP variance as change in insight (-1.7 PSP point/insight point) as well as change in negative symptoms (-0.7 PSP point/negative symptom point), and treatment duration (0.8 PSP point/month).

Conclusion: These findings support a relationship between insight, duration of treatment, and social functioning. The interaction between insight, cognition, and overall functioning will be discussed.

Sponsored by Janssen, LP.

References:

1. Goodman C, Knoll G, Isakov V, Silver H: Insight into illness in schizophrenia. Compr Psychiatry 2005;46:284-290.

2. Rossell SL, Coakes J, Shapleske J, Woodruff PW, David AS. Insight: its relationship with cognitive function, brain volume and symptoms in schizophrenia. Psychol Med 2003;33:111-119.

NR351 Tuesday, May 23, 12:00 PM - 2:00 PM

Differential Effects of Various Antipsychotics on Plasma Glucose and Insulin Levels in the Mouse

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Educational Objectives:

At the conclusion of this presentation, the participants will be able to (1) gain insight into the utility of an animal model to study metabolic liabilities of antipsychotic compounds, (2) better understand the differential glycemic effects of various, clinically used antipsychotics.

Summary:

Introduction: Treatment with some, but not all, atypical antipsychotics has been associated with weight gain, hyperglycemia, lipid abnormalities and the development of type II diabetes in patients. The aim of these studies was to characterize the acute effects of various typical and atypical antipsychotic drugs on plasma glucose and insulin levels in mice.

Methods: Male FVB/N mice received a single, intraperitoneal injection of an antipsychotic drug or vehicle. Blood samples were collected via retro-orbital bleeding at 1h or 3h post-dose. Plasma glucose and insulin were measured by enzymatic (Roche Autoanalyzer) and ELISA methods, respectively.

Results: Administration of clozapine (20 mg/kg), olanzapine (5 mg/kg), quetiapine (10 mg/kg), perphenazine (10 mg/kg) and chlorpromazine (10 mg/kg) induced significant increases in plasma glucose by 140, 98, 97, 120 and 144% above basal levels, respectively. In contrast, ziprasidone (10 mg/kg), aripiprazole (20 mg/kg), and haloperidol (2 mg/kg) did not significantly alter glucose levels. Risperidone (2 mg/kg) reduced plasma glucose (-30%) via marked enhancement of insulin release. None of the other drugs had significant effect on insulin. Subsequent dose-response studies (1, 3 and 10 mg/kg) on selected compounds revealed that clozapine and olanzapine induced significant elevation of glucose at doses of 3 and 10 mg/kg, while ziprasidone did not induce hyperglycemia at any doses tested.

Conclusion: These data indicate that glycemic effects of antipsychotics in mice may be predictive of clinical liability since drugs that produced marked hyperglycemia in mice have been linked to glucose dysregulation and the development of diabetes in patients.

References:

1. Newcomer JW. Abnormalities of glucose metabolism associated with atypical antipsychotic drugs. J Clin Psychiatry. 2004; 65 Suppl 18:36-46.

2. Dwyer DS, Donohoe D. Induction of hyperglycemia in mice with atypical antipsychotic drugs that inhibit glucose uptake. Pharmacol Biochem Behav 2003; 75(2):255-60.

NR352 Tuesday, May 23, 12:00 PM - 2:00 PM

Metabolic Studies of Patients With Schizophrenia on Atypical Antipsychotics

Ira D. Glick, M.D. *Stanford University School of Medicine, Psychiatry, 401 Quarry Road, Suite 2122, Stanford, CA, 94305-5723*, Gerald M. Reaven, Sr., M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand and manage metabolic effects of atyical antipsychotics for patients with schizophrenia

Summary:

Objective: Although atypical antipsychotics have become the standard of care for schizophrenia, there have been major concerns about the growing body of evidence linking these medications to metabolic problems related to excessive weight gain. Accordingly, the study had two objectives - 1) quantification of insulin-mediated glucose disposal in overweight patients being treated with atypicals (SGAs), and 2) to determine if patients who had gained weight and were clinically stable, would/could switch to aripiprazole, and what would happen to their weight and degree of insulin resistance.

Methods: This was an open-label, pilot study with 20 overweight patients with schizophrenia, who had stabilized on either clozapine, olanzapine, risperidone or quetiapine. Patients were weighed at baseline, tested with a standard psychiatric battery, and a specific measurement of insulin-mediated glucose disposal performed. Following these determinations, patients were slowly tapered from their antipsychotic, started on flexible dosing of aripiprazole (15-30 mg), and evaluated monthly for four months.

Results: We enrolled 20 patients. Of these, 4 were dropouts. Of the remaining 16 chronic patients, 6 could not be tapered off their clozapine (3), olanzapine (2), or quetiapine (1). The remaining 10 were successfully switched.

Clinically, all 10 patients did as well or improved on aripiprazole compared to their prior antipsychotic. Although the study is not yet concluded, 7 of 9 have lost weight. Of the first 11 patients (tested before switching), we found that 3 were insulin sensitive, 7 insulin-resistant, while 1 reading was intermediate.. After switching to aripiprazole, 5 (of 9) patients showed improved insulin sensitivity, whereas 4, were more insulin resistant.

Summary and Conclusions: We have learned that 1) there is a wide range of insulin sensitivity in obese patients treated with SGAs, and 2) weight loss does not necessarily mean that insulin sensitivity will improve.

References:

1. Davis JM, Chen H, Glick ID: A meta-analysis of the efficacy of second-generation antipsychotics. Archives of General Psychiatry 2003; 60:553-564.

2. Nasrallah HA, Newcomer JW: Atypical antipsychotics and metabolic dysregulation: evaluating the risk/benefit equation and improving the standard of care. J Clin Psychopharmacol 2004;24:S7-S14.

NR353 Tuesday, May 23, 12:00 PM - 2:00 PM

Lamotrigine Added to Atypical Antipsychotics for Treatment of Schizophrenia: Results of Two Double-Blind Randomized Clinical Trials

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to demonstrate, an understanding of the methods and results of two randomized, double-blind, clinical trials evaluating lamotrigine as add-on therapy to atypical antipsychotics in schizophrenia.

Summary:

Introduction: Despite treatment with atypical antipsychotics, many patients with schizophrenia experience persistent symptoms. A prior human laboratory study found that lamotrigine reduced symptoms and cognitive impairments associated with schizophrenia in the ketamine model of psychosis and prior reports in controlled clinical trials suggested that lamotrigine might improve psychopathology when added to ongoing antipsychotic treatment.[1,2]

Objective: To evaluate the efficacy of lamotrigine as adjunctive therapy to atypical antipsychotics in schizophrenia.

Method: Two 12-week, multicenter, randomized, double-blind, placebo-controlled studies (SCA30926 [N=209] and SCA101464 [N=210]) evaluated lamotrigine (100- 400 mg/day) in schizophrenia patients maintained on atypical antipsychotics. Outcome measures included the PANSS for psychopathology and the Brief Assessment of Cognition for Schizophrenia (BACS) for neurocognitive deficits.

Results: No significant differences in the primary outcome measure, mean decrease in total PANSS score, were observed between placebo and lamotrigine groups in either study. In SCA30926, the mean PANSS score decreased -8.2 (se=1.35) versus -6.0 (se=1.35) placebo and lamotrigine, respectively (P = 0.19). In SCA101464, the mean PANSS score decreased -12.0 (SE=1.21) versus -12.9 (SE=1.21), placebo and lamotrigine, respectively (P=0.59). In SCA101464, the BACS composite score improved by 0.44 (se=0.06679) for lamotrigine versus 0.20 (se=0.069) for placebo (P=0.011). More BACS responders (> or = 0.5 z-score improvement) received lamotrigine than placebo (43.0% versus 28.4%, P=0.038); no difference was found in SCA30926. No unexpected adverse events or serious rashes were reported.

Conclusions: Lamotrigine, when added to atypical antipsychotics did not demonstrate efficacy in the treatment of residual psychopathological symptoms in patients with schizophrenia; but showed improvement in cognition in one of two studies. Lamotrigine was well tolerated.

References:

1. 1. Tiihonen J, Hallikainen T, Ryynanen O-P, Repo-Tiihonen E, Kotilainen I, Eronen M, Toivonen P, Wahlbeck K, Putkonen A. Lamotrigine in treatment-resistant schizophrenia: a randomized placebo-controlled crossover trial. Biol Psychiatry. 2003;54:12.

2. 2. Kremer I, Vass A, Gorelik I, Bar G, Blanaru M, Javitt DC, Heresco-Levy U. Placebo-controlled trial of lamotrigine added to conventional and atypical antipsychotics in schizophrenia. Biol Psychiatry 2004;56(6):441-6.

NR354 Tuesday, May 23, 12:00 PM - 2:00 PM

Psychosocial Assessment in Families and Caregivers of Patients With Childhood Onset Schizophrenia: A Study From India

Savita Malhotra, M.D. *Chandigarh, India*, Nitin Gupta, M.D., Mehak Kapoor, M.A., Sapna Gill, M.A.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to demonstrate [1] the need for and relevance of cross-cultural research in schizophrenia, especially in this rare entity of childhood onset schizophrenia, and [2] the importance of as-

sessing caregivers/family members of patients with childhood onset schizophrenia as they suffer from considerable dysfunction and burden so that professionals can develop management strategies in the overall care package for persons suffering with childhood onset schizophrenia.

Summary:

Objective: Caregivers of patients with adult onset schizophrenia (AOS) experience considerable dysfunction and burden of care. Childhood onset schizophrenia (COS) is a chronic, severe form of AOS with poor outcome. Due to lack of data, this study was planned with the objective of assessing the psychosocial aspects aspects of caregivers of these patients from India.

Methods: A cross-sectional study was carried out where 14 cases with ICD-10 diagnosis of schizophrenia (age at onset < 14 years of age) were assessed on socidemographic and clinical profile sheet, Family Coping Questionnaire by Magliano et al, 1996; Camberwell Assessment of Needs by Phelan et al, 1995; Burden Assessment Schedule by Thara et al, 1998; and Dysfunction Analysis Questionnaire by Pershad et al, 1985.

Results: The mean age of caregivers was 45.9 years, 65%being males, 70% with >10 educational years, 64% from nuclear families and 79% of urban background. High dysfunction was perceived in all domains (social, vocational, physical, functional, cognitive). Maximum burden of care was seen in areas of physical and mental health, taking up responsibility. Educational, marital and relationship needs were fulfilled; no focus on personal/biological functions of the patient, and unfulfilled needs for finances, occupation and treatment were reported. Varied coping styles were utilised, more commonly emotion-focussed than problem-focussed.

Conclusions: COS imposes considerable dysfunction and burden on the caregivers whose certain needs require fulfilment. Coping styles utilised were on lines as for AOS indicating that caregivers require equal focus during the management of patients with COS.

Funding: This study was carried out as part of the PGI Research Scheme entitled "To study the course and outcome of childhood onset schizophrenia" and was supportedby funding provided by Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, India.

References:

1. Dixon L, Lehman AF: Family interventions for schizophrenia. Schizophr Bull 1995; 21: 631-643.
2. Leiberman JA, Murray RM: Comprehensive care of schizophrenia: A textbook of clinical management. Martin Dunitz, London, 2001.

NR355 Tuesday, May 23, 12:00 PM - 2:00 PM

Cell Phone Dependence in Adolescence: A Preliminary Study

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Educational Objectives:

Cell phone becomes a necessity in the modern home. Entering the ubiquitous world, cell phone starts to provide various kinds of services including TV, games, and internet. Now it is unthinkable to live without cell phones, then sometimes we easily feel anxiety when going out without it. People already have been experiencing psychological dependence. However we do not know clearly the existence of cell phone dependence. We planned a preliminary study to identify the psychological dependence to cell phone implying a self-rating questionnaire developed by authors. At the conclusion of this presentation, participants should be able to understand the psychological meaning of cell phone to adolescent and possible psychopathology related to cell phone dependence.

Summary:

Object: The object of this study is to evaluate the possible psychological problems related to cell phone dependence in adolescence.

Method: 595 high school students (male=552 female=42, mean age=15.9±0.8 years) were recruited. Cell phone dependence was evaluated by 20 item self-report questionnaire developed by authors. It contains items about communication wishes, identification themselves with cell phone, and difficulty in control. Cell phone using patterns and psychopathology were evaluated between upper 30% and lower 30% group according to score by the questionnaire.

Results: Possible cell phone dependence group called and received phone more than lower group, especially using text messages. They had tendency to identify themselves with cell phone, wish to persist connection with others regardless of situation, and have difficulties in controlling usage. They showed higher score in Beck depression inventory (12.3±8.4 versus 7.3±6.6, F=14.60, p<0.0001), interpersonal anxiety scale (41.3±9.4 versus 37.4±3.7, F=12.95, p<0.0001), and lower score in Rosenberg self-esteem scale (32.7±6.8 versus 35.2±6.0, F=1.29, p<0.0001). Positive correlation was observed between cell phone dependence and internet addiction (partial r =0.27).

Conclusion: Current findings suggest that the psychological dependence to cell phone can be related to the mental health problems. Careful guide and evaluation are needed in using a cell phone in adolescence.

References:

1. Bianchi A, Phillips JG. Psychological predictors of problem mobile phone use.Cyberpsychol Behav. 2005 Feb;8(1):39-51.
2. Adam Burgess: Cellular Phones, Public Fears, and a Culture of Precaution. London, Cambridge University Press, 2003.

NR356 WITHDRAWN

NR357 WITHDRAWN

NR358 Tuesday, May 23, 12:00 PM - 2:00 PM

A Cross-Sectional Study of Adiponectin in Patients With Schizophrenia

Linda Hanssens, M.S. *University Liege, CHU Sart Tilman, Liege, B 4000, Belgium*, Marc De Hert, M.D., Dominique Van Eyck, M.F.A., Martine Wampers, Psy.D., Andre Scheen, Prof. Dr., Jozef Peuskens, Prof. Dr.

Educational Objectives:

At the conclusion of this presentation the participant should understand the role of adiponectin in the regulation of glucose homeostasis in patients treated with antipsychotic medication.

Summary:

Background: Adiponectin is a recently identified adipocyte-derived protein associated with metabolic abnormailities such as obesity, insulin resistance and diabetes. Metabolic disorders are a growing concern in patients treated with antipsychotic medication.

Methods: Fasting adiponectin levels were assessed in a cross-sectional sample of 294 patients with schizophrenia treated with antipsychotic medication. The patients are enrolled in a prospective study evaluating the metabolic effects of antipsychotics. All underwent an extensive metabolic screening, including an oral glucose tolerance test.

Results: Adiponectin levels are correlated with BMI, and differ significantly between patients with normal weight, overweight or obesity (p=0.0001). Patients meeting criteria for the metabolic syndrome, either with NCEP ATP-III criteria (28.2%) or with the more recent IDF criteria (35.7%), have significantly lower adiponectin levels than patients without a metabolic syndrome (p= 0.0001). Patients without glucose abnormalities (82.7%) have significantly higher adiponectine levels compared to patients with glucose abnormalities (IFG and/or IGT, 9.9%) or patients meeting ADA criteria for diabetes (7.5%) (p=0.004). Adiponectin levels are lowest in diabetic patients.

After controlling for BMI, antipsychotic medication significantly influences adiponectin levels (p<0.01). Adiponectin levels are significantly lower (p<0.05) in patients treated with olanzapine.

Conclusions: In schizophrenic patients, adiponectin levels vary in the same way as described in the normal, overweight and obese non schizophrenic population. Also, adiponectin levels in schizophrenic patients with and without metabolic syndrome mirror what is observed in the general population. Preliminary data suggests that the antipsychotic treatment may influence adiponectin regulation, a finding that should be verified in longitudinal studies.

Acknowledgement: Educational grant from global epidemilogy and outcomes research (GEOR) BMS

NR359 Tuesday, May 23, 12:00 PM - 2:00 PM

Evaluation of Quality of Life in Community-Treated Schizophrenic Patients: A Naturalistic Open-Label Study Comparing Aripiprazole to Standard-of-Care

Linda Hanssens, M.P.H. *Bristol Myers Squibb Braine-l'Alleud, Parc De L'Alleud, Braine L' Alleud, Belgium*, Gilbert L'Italien, Ph.D., Ronald N. Marcus, M.D., Robert D. McQuade, Ph.D., William H. Carson, Jr., M.D., Jean-Noel Beuzen, M.D.

Educational Objectives:

Participants in this session will learn that the choice of antipsychotic agent may have an impact on patient reported outcomes.

Summary:

Background : Naturalistic trials allow clinicians to assess patient reported outcomes in real life settings. In this study, general quality of life among schizophrenic outpatients was assessed and compared between aripiprazole and standard of care agents.

Methods: 555 patients were equally randomized to either aripiprazole(10-30 mg/day) or Standard-of-Care (olanzapine 5 - 20 mg/day, or quetiapine 100 - 800 mg/day or risperidone 2 - 8 mg/day) Clinicians were free to choose the most appropriate Standard-of-Care medication for their respective patients. Quality of life was evaluated by the Quality of life Scale(QLS), a validated instrument designed to evaluate the current functioning of non hospitalized schizophrenic patients and the intrapsychic domains impacted by negative symptoms. QLS assesses four domains: Interpersonal Relations, Instrumental Role, Intrapsychic Foundations and Common Objects and Activities. A total score and 4 subscale scores are derived from item specific scores; higher scores reflect better QOL.

Results: The mean change from baseline in the QLS Total score at Week 26 LOCF was 8.17 ± 1.24 in the aripiprazole group and 3.22 ±1.31 in the SOC group, the difference between groups is statistically significant in favor of aripiprazole(p<0.001). The mean change from baseline in the 4 subscale Scores: Interpersonal Relations, Instrumental Role, Intrapsychic Foundations and Common Objects and Activities are all statistically significant different in favor of the aripiprazole treated group: p=0.006,p=0.005, p< 0.001and 0.025 respectively.

Conclusion.: Patients treated with aripiprazole showed a statistically significant larger improvement in QLS total and subscale score than patients treated with SoC. Impact of therapies on patient quality of life can be a strong determinant of the acceptability of a given treatment and might ultimately lead to better compliance and overall satisfaction with care.

References:

1. Ritsner M, Kurs R, Ratner Y, Gibel A. Condensed version of the quality of life scale for schizophrenia for use in outcomes studies. Psychiatry Res 2005;135(1):65-75.

2. Heinrichs DW, et al. the Quality of Life Scale: An instrument for rating the Schizophrenia defict Syndrome.Schizophrenia Bulletin 1984; 10(3):388-398.

NR360 Tuesday, May 23, 12:00 PM - 2:00 PM

Reasons for Switching Among Community-Treated Schizophrenic Patients in a Naturalistic setting Schizophrenia Trial of Aripiprazole: STAR Study

Linda Hanssens, M.P.H. *Bristol Myers Squibb Braine-1Alleud, Parc De L'Alleud, Braine L' Alleud, Belgium*, Gilbert L'Italien, Ph.D., Ronald N. Marcus, M.D., Robert D. McQuade, Ph.D., William H. Carson, Jr., M.D., Jean-Noel Beuzen, M.D.

Educational Objectives:

At the completion of the session, participants will gain an understanding of the principal determinants of a change in antipsychotic regimen

Summary:

Background : Naturalistic studies offer both clinicians and patients an opportunity to provide feedback as to the quality of therapeutic care in terms of efficacy, tolerability, and safety (ie effectiveness). The STAR study aimed at comparing the effectiveness of aripiprazole and Standard of Care (SOC) in community treated schizophrenic patients

Methods: 555 patients were equally randomized to either aripiprazole(10-30 mg/day) or Standard of Care. Clinicians were free to choose the most appropriate Standard of Care medication (olanzapine 5 - 20 mg/day, or quetiapine 100 - 800 mg/day or risperidone 2 - 8 mg/day) for their respective patients.. Information on both the patients' prior regimen and reason for changing antipsychotic medication was collected.

Results : Prior medications included olanzapine (22%), risperidone (19%), both as monotherapy, other single atypicals (20%), polypharmacy (22%) and single typicals (14%). The major primary reasons for changing medication were negative symptoms (29%), positive symptoms (27%), lack of energy (6%), cognitive dysfunction (5%), weight gain (12%), EPS other than akathisia (6%) .

Conclusion : In a naturalistic setting, suboptimal efficacy remains the primary reason for change in regimen in about half of the patients. However, tolerability and safety issues, in particular weight gain are important secondary determinants of therapeutic switches. Since medication changes may impact compliance and threaten relapse, the choice of appropriate agent remains the highest priority for treating physicians

References:

1. Tandon R, DeVellis R, Han J, Li H, Frangou S, Dursun S. Validation of the Investigators Assessment Questionnaire, a new clinical tool for relative assessment of response to antipsychotics in patients with schizophrenia and schizoaffective disorder. P.

2. Guidance on the use of newer (atypical) antipsychotic drugs for the treatment of schizophrenia: National institute for Clinical Excellence;2002.

NR361 Tuesday, May 23, 12:00 PM - 2:00 PM

Sexual Dysfunction in a Naturalistic Open Label Study of Aripiprazole and Standard of Care in the Management of Community-Treated Schizophrenic Patients

Linda Hanssens, M.P.H. *Bristol Myers Squibb Braine-1Alleud, Parc De l'Alliance 8, Braine L' Alleud, Belgium*, Gilbert L'Italien, Ph.D., Ronald N. Marcus, M.D., Robert D. McQuade, Ph.D., William H. Carson, Jr., M.D., Jean-Noel Beuzen, M.D.

Educational Objectives:

At the completion of this session, participants will gain an understanding of the differential effects of atypical antipsychotics on sexual dysfunction via drug induced hyperprolactinemia

Summary:

Background : Naturalistic trials allow clinicians to assess patient reported outcomes in real life settings. In this study, sexual dysfunction of schizophrenic outpatients was assessed and compared between aripiprazole and Standard of Care agents.

Methods: 555 patients were equally randomized to either aripiprazole(10-30 mg/day) or Standard of Care. Clinicians were free to choose the most appropriate Standard of Care medication (olanzapine 5 - 20 mg/day, or quetiapine 100 - 800 mg/day or risperidone 2 - 8 mg/day) for their respective patients. Sexual dysfunction was evaluated using the validated Arizona Sexual Experience Scale (ASEX) (1). The scale measures 5 items for males and females separately: sex drive, arousal, vaginal lubrication/penile Extended Release ection, ability to reach orgasm and satisfaction from orgasm. Total scores range from 5 to 30 with higher scores indicating more sexual dysfunction. Concurrent with these evaluations, serum prolactin levels were also measured, since these may be correlated with sexual dysfunction (2)

Results: The mean change from baseline in the ASEX total score was -1.44±0.31 in the aripiprazole group and -0.56±0.34 in the Standard of Care group at 26 weeks LOCF. These results show a statistically significant difference in sexual functioning in favor of aripiprazole treated patients (p=0.012). The proportion of patients with potentially clinically significant abnormal serum prolactin levels was 16.8 % in the aripiprazole group versus 54.4% in the SOC group (p<.001). The mean change from baseline in serum prolactin was -32.1±1.8 in the aripiprazole group and -12.3±1.9 in the SOC group(26 weeks LOCF p< 0.001)

Conclusion: Based on the ASEX, patients treated with aripiprazole demonstrated an improvement of their sexual function consistent with a significantly improvement in serum prolactin levels compared to Standard of Care patients.

References:

1. McGahuey CA et al The Arizona Sexual Exeprience Scale (ASEX): Reliability and Validity. Journal of sex & Marital Therapy 2000;26:25-40.
2. Guidance on the use of newer (atypical) antipsychotic drugs for the treatment of schizophrenia: National institute for Clinical Excellence;2002.

NR362 Tuesday, May 23, 12:00 PM - 2:00 PM

Eye Movements and Neuregulin-1 Risk Genotype in Schizophrenia

Magnus Haraldsson, M.D. *Landspítali-University Hospital, Psychiatry, Skildinganes 14, Reykjavik, 101, Iceland*, Ulrich Ettinger, Ph.D., Brynja B. Magnusdottir, B.A., Thordur Sigmundsson, M.D., Engilbert Sigurdsson, M.D., Hannes Petursson, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the role of smooth pursuit and antisaccade eye movements as potential endophenotypes in genetic research of schizophrenia. In the presented study the performance on these eye movement tasks were compared in groups of schizophrenia patients and healthy controls with and without the at risk Neuregulin-1 haplotype.

Summary:

Several recent studies provide evidence that variations in the Neuregulin-1 gene (NRG-1) influence the risk for schizophrenia. Eye movements and other potential endophenotypes in individuals with and without NRG-1 variations may help explaining the role of NRG-1 polymorphisms in the pathogenesis of schizophrenia.

The aim of this study is to investigate the effects of the Icelandic "5 SNP at-risk" core haplotype of NRG-1 on smooth pursuit eye movements (SPEM) and the antisaccade task (AS) in Patients with Schizophrenia and controls.

We have tested 39 schizophrenic patients (17 with and 22 without the NRG-1 "at risk" haplotype) and 27 healthy controls (11 with and 16 without the haplotype). Participants underwent infrared oculographic assessment of antisaccades and smooth pursuit (at 0.25, 0.5, and 0.75Hz).

Preliminary findings consistantly suggest a trend towards the NRG-1 at risk patient group having a slower SPEM gain than patients without the "at-risk" haplotype at target velocities 0.50 and 0.75 Hz (Cohen's d=0.26 and 0.29, respectively). There was also a trend towards controls with the "at risk" haplotype having a slower SPEM gain than controls without the haplotype at all target velocities. Furthermore, there was a trend towards controls with the haplotype having more AS Extended Release rors, impaired AS gain and a longer AS latency than controls without the haplotype (Cohen's d=0.32-0.48).

In this first study of effects of NRG-1 polymorphism on eye movements preliminary findings suggest that the NRG-1 "at risk" haplotype may have adverse effects on eye movements. Testing continues in patients and controls to examine this further

References:

1. Harrison PJ, Weinberger DR: Schizophrenia genes, gene expression, and neuropathology: on the matter of their convergence. Mol Psychiatry. 2005;10(1):40-68.
2. Calkins ME, Iacono WG, Curtis CE: Smooth pursuit and antisaccade performance evidence trait stability in schizophrenia patients and their relatives. 2003;49(2):139-46.

NR363 Tuesday, May 23, 12:00 PM - 2:00 PM

Transition into Primary-care Psychiatry (TIPP): The Feasibility of Conducting a Full-Scale Cluster Randomization Study

David Haslam, M.D. *Regional Mental Health Care London, Collaborative Mental Health Care, 850 Highbury Ave North, P.O. Box 5532 Station B, London, ON, N6A 4H1, Canada*, Jack Haggarty, M.D., Jatinder Takhar, M.D.

Educational Objectives:

Determine the feasibility of conducting a large-scale trial to evaluate the Transition into Primary-care Psychiatry (TIPP) program effectiveness on quality of life, symptomatology, perceived need for care, and economic outcomes.

Summary:

Objectives

Determine the feasibility of conducting a large-scale trial to evaluate the Transition into Primary-care Psychiatry (TIPP) pro-

gram effectiveness on quality of life, symptomatology, perceived need for care, and economic outcomes.

Study Design

Eighteen month cluster randomization feasibility trial comparing the TIPP service to care-as-usual. The TIPP service is provided for people whose mental health care is being transitioned from secondary and tertiary services to ongoing follow-up with their family physician (FP). TIPP service includes co-location in FP offices, psychiatrist consultation, psychiatric nurse care, client monitoring system, and telephone back up. Secondary and tertiary services, as well as FP offices, are located in Southwestern and Northwestern Ontario. Primary outcome measure is the Quality of Well Being Scale. Tools used to derive secondary outcomes are the Brief Symptom Inventory, Perceived Needs for Care, Family Burden Scale, and resource utilization cost measures.

Principal findings

Health care delivery system factors resulted in interim data being only recently obtained for study participants (N=26 and 20) using outpatient psychiatry services (N=2 and 1) and their FPs (N=16 and 9) in Southwestern and Northeastern, Ontario, respectively. Significant early challenges have included stakeholder acceptability of an experimental evaluation model, adequate recruitment, inter-site service variability, as well as factors contributing to selection, performance, and exclusion and detection bias.

Conclusion

The TIPP project will provide the basis for determining the feasibility of a large-scale trial and inform future initiatives endeavoring to determine the effectiveness collaborative mental health care services using a multi-site cluster randomization methodology

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References:

1. Donner A, Klar N: Design and analysis of cluster randomization trials in health research. London: Arnold 2000.
2. Meadows GN: Overcoming bariers to reintegration of patients with schizophrenia: developing a best-practice model for discharge from specialist care. Med J Aust 2003; 178(Suppl): S53-6.

NR364 Tuesday, May 23, 12:00 PM - 2:00 PM

Diabetes Screening, Risk Management and Disease Management in a High-Risk Mental Health Population: An Evaluation Project

David Haslam, M.D. *Regional Mental Health Care London, Collaborative Mental Health Care, 850 Highbury Ave North, P.O. Box 5532 Station B, London, ON, N6A 4H1, Canada*, Stewart Harris, M.D., Barbara Lent, M.D., Betty Harvey, M.S.N., Tamara Biederman, Ph.D.

Educational Objectives:

At the end of this session, participants will be able to understand how an innovative program is providing a screening and management program for people with mental illness at high risk for diabetes, understand the outcome measures selected to evaluate this innovative clinical service, and know the results of the projects outcome measures.

Summary:

The disorder of schizophrenia has been repeatedly associated with a higher than normal incidence of medical illnesses- specifically, diabetes. In addition, the first line treatment of Schizophrenia as per published clinical practice algorithms, novel antipsychotics (NAP), has been associated with increased risk for diabetes. Accordingly, this high-risk group requires a targeted primary health care service delivery model that attends to the unique set of diabetes-related challenges. To determine how these complex patients are currently being managed, an audit of primary care charts was conducted for people identified through an urban Ontario community mental health service database as being diagnosed with schizophrenia and/or prescribed a novel antipsychotic medication. Physician participation in this portion of the project was difficult to gain and results demonstrate low frequency of appropriate diabetes screening. The current project also piloted a diabetes screening and disease management model for this high-risk group. In partnership with community service providers, OGTT screening and multidisciplinary management clinics were conducted at usual point of services for this population. Events were well attended and 20% of participants screened were found to have previously undiagnosed diabetes or a pre-diabetic condition. Clinically significant changes in participants' disease markers such as HbA1c, BMI, and blood pressure were also found. Stakeholder feedback and lessons learned regarding creating a shared care model with physicians and community providers are also valuable outcomes of this pilot project.

References:

1. Brown JB, Lent B, Stirling A, Takhar J, BishopJ: Caring for seriously mentally ill patients. Can Fam Phys 2002; 48:915-920.
2. CDA Clinical Practice Guidelines Expert Committee: CDA 2003 Clinical Practice Guidelines for the preventiona nd managemnet of diabetes in Canada. Can J Diabetes 2003; 27 (Suppl 2).

NR365 Tuesday, May 23, 12:00 PM - 2:00 PM

Cognitive and Symptomatic Correlates of Functional Capacity in Schizophrenia-Related Disorders

R. Walter Heinrichs, Ph.D. *York University, Psychology, 4700 Keele Street, Toronto, ON, M3J 1P3, Canada*, Meghan Kirsch, B.A., Parvaneh Moallef, M.A., Diana Smith, B.A., Marta Statucka, B.A., Susan Strong, M.S., Panth Voruganti, M.D.

Educational Objectives:

At the conclusion of the session, the participant should be able to recognize clinical and cognitive features that associate with impaired and more preserved everyday living skills in schizophrenia patients.

Summary:

Objective: To assess cognitive and symptomatic correlates of functional capacity in clients with schizophrenia and related conditions using recent advances in life skills assessment.

Method: Demographic, clinical and cognitive data were obtained on n = 29 community-dwelling clients who met DSM-IV criteria for schizophrenia or schizoaffective disorder. Functional capacity was measured with the University of California Performance Skills Assessment (UPSA; Patterson et al., 2001) modified for Canadian settings. The UPSA uses role-play and prop materials and comprises demonstration of skills in 6 domains of basic living: comprehension and planning, finance, communication, transportation, household management and medication management.

Results: The summary index of UPSA performance was unrelated to demographic variables (age, sex, education) or positive symptoms (Positive and Negative Symptom Scale; PANSS). However, overall functional capacity did vary significantly with general psychopathology ($r = -.39$; $p \leq .05$; PANSS) and negative symptoms ($r = -.40$; $p \leq .05$;PANSS) and with cognitive measures of verbal ability ($r = .61$; $p \leq .001$), reasoning ($r = .39$; $p \leq .05$),working memory ($r = .39$,$p \leq .05$) and processing speed ($r = .40$; $p \leq .05$)(Wechsler Adult Intelligence Scale;WAIS-III). Verbal memory (California Verbal Learning Test;CVLT-II) was not related to UPSA scores.

Conclusions: Performance-based assessment of life skills is more objective and observationally grounded than either patient

self-report or clinician ratings. Hence, these assessment data provide an important perspective on functional outcome in schizophrenia. Psychological distress and negative symptoms, verbal ability, analytical reasoning and processing speed may be key predictors of functional status in schizophrenia. In contrast, psychotic symptoms and current verbal memory abilities may not relate to this aspect of outcome. This research is supported by The Ontario Mental Health Foundation.

References:

1. Patterson TL, Goldman S, McKibbin CL, Hughs T, Jeste DV: UCSD Performance-based skills assessment: development of a new measure of everyday functioning for severely mentally ill adults. Schizophr Bull 2001; 27: 235-245.
2. McKibbin CL, Brekke JS, Sires D, Jeste DV, Patterson TL: Direct assessment of functional abilities:relevance to persons with schizophrenia. Schizophr Res 2004; 72:53-67.

NR366 Tuesday, May 23, 12:00 PM - 2:00 PM

Association Study Between a Functional NAD(P)H: Quinone Oxidoreductase (NQO1) Gene Polymorphism (Pro187Ser) and Tardive Dyskinesia

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to demonstrate clinical implications.

Summary:

Several lines of evidence have indicated that free radicals may play a role in the pathophysiology of tardive dyskinesia (TD) (reviewed in Lohr et al, 2003). NAD(P)H: quinone oxidoreductase (NQO1) is an important enzyme in the human body that counteracts the oxidative stress-induced neuronal injury caused by the toxic free radicals such as dopamine-semiquinones. Taking the possible genetic predisposition to TD into account (Yassa and Ananth, 1981), the NQO1 gene is a good candidate gene that may confer increased susceptibility to TD. Based on this hypothesis, Pae et al. (2004) reported a significant association between the Pro187Ser polymorphism in the NQO1 gene and TD. In the present study, we attempted to replicate the findings of Pae et al. (2004) with the same polymorphism in 222 Japanese patients with schizophrenia. No significant difference was detected between patients with and without TD in the allelic distribution ($\chi^2 = 0.070$, d.f. = 1, $p = 0.795$) and in the genotypic distribution ($\chi^2 = 0.910$, d.f. = 2, $p = 0.657$). In addition, there was no significant difference in terms of total AIMS scores among the three genotype groups ($p = 0.49$). Our results suggest that the NQO1 gene polymorphism does not confer an increased risk of TD.

References:

1. Lohr et al., 2003.
2. Yassa and Ananth, 1981.

NR367 Tuesday, May 23, 12:00 PM - 2:00 PM

Choosing a Form of Antipsychotic Medication

Johannes E. Hovens, Ph.D. *Delta Psychiatric Center, Taeching Department, Vondellaan 19, Leiden, 2332 AA, The Netherlands,* Beatriz Roman, M.Psy., Renier van Dinter, Dr. Med. Sc.

Educational Objectives:

At the conclusion of this presentation, the participant should know the the attitudes of psychiatrists and patients to antipsychotic medication.

Summary:

Objective: Long-acting antipsychotic medication has a number of advantages, such as treatment adherence, lower peak plasma levels, and a reduction in relapse rates (Davis et al., 1995). However, less than 20% of the patients on maintenance antipsychotics receive a long-acting injection. The objective of this study is to gain insight into the choice process for an administration form.

Method: Interviews were conducted with 92 outpatient patients with a chronic psychotic disorder and with 14 psychiatrists, involved in evaluating antipsychotic medication treatments.

Results: Psychiatrists (100%) and patients (91%) stated that the choice for a form of administration should be made in consultation between patient and physician. In practice the psychiatrist makes the choice. The psychiatrists unanimously stated a preference for the 'regular' daily tablets, based on the expectation that patients would prefer this. Yet they mentioned significantly more advantages of long-acting injections. In all patient groups, the trade-off between arguments in favour and against depot medication was resolved favourably for depot-medication.

Conclusion: psychiatrists hold a biased view regarding patients' opinions of depot antipsychotics. As they expect patients to have a negative attitude towards injections, they often make it a 'last resort' option.

References:

1. Davis, JM, Wang, Z and Janicak, PG (1995) Depot versus oral maintenance in schizophrenia: a meta-analysis of mirror-image studies. Schizophrenia Research, 15:148.
2. Patel, MX, Nikolau, V. and David, AS (2003). Psychiatrists' attitudes to maintenance medication for patients with schizophrenia. Psychological medicine, 33: 83-89.

NR368 Tuesday, May 23, 12:00 PM - 2:00 PM

Patients with Schizophrenia Favour Long-Acting Antipsychotic Medication

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Educational Objectives:

At the conclusion of this presentation, the participant should know that patients with schizophrenia prefer long-acting antipsychotic medication.

Summary:

Objective: Patients' lack of adherence to their maintenance treatment with antipsychotic medication represents a major setback for the optimal treatment of psychotic disorders (Gilbert et al, 2004). By administering antipsychotic medication through a long-acting injection instead of using daily oral forms, non-compliance rates can be reduced. In practice, however, only a small minority of patients receive antipsychotics in this way. Recent research has shown that psychiatrists have a negative attitude towards the use of long-acting injections, which are often considered 'stigmatising' and 'old-fashioned' (Patel et al., 2003). They also expect their patients to have similar negative attitudes. To date, 'patients' views on this subject have not been studied. This study's purpose is thus to gain insight into patients' opinion regarding the different administration forms for maintenance treatment with antipsychotic medication. Method: Individual semi-structured in-depth interviews were conducted with 92 patients, selected from

a non-proportional convenience sample to contain patients from the different medication categories: conventional oral (n=13), atypical oral (n=40), conventional injected (n=20) and atypical injected (n=19) antipsychotics as current medication. All patients were 18 or older and participated voluntarily. The following selection criteria were used: - Diagnosis of a chronic psychotic disorder, preferably schizophrenia; - Ambulant maintenance treatment with antipsychotics; - Symptoms that allow participation in the interview. Results: When asked for their preferences, an equal number of patients chose long-acting injections as first choice treatment (n= 27) in comparison with the 'regular' daily tablets (n=28) and orodispersible tablets (n=28). 20% of the people who stated a preference for the injection were receiving an oral antipsychotic. Besides, the patients spontaneously stated significantly more advantages of long-acting injections (148 positive statements), than of tablets (104 positive statements), while at the same time mentioning slightly more disadvantages of tablets (117 negative statements) than of long-acting injections (103 negative statements). Positive statements regarding tablets included arguments that would be considered negative from a strictly clinical viewpoint, e.g. being able to experiment with the dose. Negative statements regarding injections in the oral-groups were besides based on incorrect information, e.g. injections cause more side-effects. Frequent arguments against the use of long-acting injections were refuted by the surveyed users: 79.5% did not find it a burden having to attend the health clinic to have the injection, 84.6% had no problems with another person administering their medications and 94.6% stated they had never skipped an injection because of fear. In general, the patients' choices were guided by the degree to which they believed the administration form would facilitate a correct medication intake: this entails choosing the administration form believed to bring the greatest ease of use and autonomy (defined by the patients as not having to think about medication). Conclusion: The large majority of patients did not have a negative attitude towards the administration of antipsychotics through a long-acting injection. The psychiatrists' expectations were thus not met. The analysis of the patients' decisional trade-off allows a more widespread use of long-acting injections for maintenance antipsychotic treatment.

References:

1. Gilmer, TP, Dolder, CR, Larro JP, Folsom DP, Lindamer, L., Garcia P, and Jeste DV. (2004) . Adherence to treatment with antipsychotic medication and health care costs among Medicaid beneficiaries with schizophrenia. American Journal Psychiatry, 161,.
2. Patel, MX, Nikolau, V. and David, AS (2003). Psychiatrists' attitudes to maintenance medication for patients with schizophrenia. Psychological medicine, 33: 83-89.

NR369 Tuesday, May 23, 12:00 PM - 2:00 PM

Comparative Role of Religion on Suicide Among Schizophrenic and Non-Psychotic Patients.

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Educational Objectives:

In this presentation, we describe the role of religion and spirituality (both in a quantitative and a qualitative perspective) on suicidal attempts among a sample of patients, both schizophrenic and non psychotic. At the conclusion of this presentation, the participants should get some indications as to how to intervene with patients suffering from schizophrenia and at risk to commit suicide.

Summary:

Objective:

A growing amount of literature suggests that religion and spirituality may provide some help to patients with schizophrenia. However, little is known about the relation between psychosis, religion and suicide.

In the present study, we investigate the role of religion and spirituality on suicidal attempts among a sample of patients, both schizophrenic and non psychotic.

Method:

One hundred and fifteen patients with psychotic disorder and 30 patients without psychotic features were interviewed. A semi-structured questionnaire assessing religiousness and spirituality was used. Past history of suicidal attempts was recorded. Possible relationship between suicidal attempts and religiousness were investigated

Results:

Religion was important in patient's lives and for coping with their disease in both samples. Forty-three percent of the psychotic patients had committed at least one suicidal attempt and there was no relationship with religious involvement. Twenty-five percent of subjects acknowledged a protective role of religion (condemnation of suicide, religious coping). Ten percent of patients reported a facilitating role of religion regarding suicidal behaviours (instillation of hope of a better outcome after death). There were no differences between groups for these results.

Conclusions:

Religion can play a significant role on suicidal behaviours, both in psychotic and non psychotic patients. Interventions aiming at lowering suicidal risks among psychiatric patients should take this dimension into account.

References:

1. Palmer BA, Pankratz VS, Bostwick JM: The lifetime risk of suicide in schizophrenia: a reexamination. Arch Gen Psychiatry 2005; 62: 247-253.
2. Huguelet Ph, Mohr S, Borras L, Gillieron C, Brandt PY: Spirituality and religious practices in outpatients with schizophrenia or schizo-affective disorders and their clinicians. Psychiatric Services (In press).

NR370 Tuesday, May 23, 12:00 PM - 2:00 PM

Memantine in the Treatment of Schizophrenic Cognitive Impairment

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to gain an understanding of the role of NMDA receptor antagonism in the treatment of cognitive impairment associated with schizophrenia

Summary:

Background

Cognitive dysfunction is a core feature of schizophrenia. Animal data, in vitro and indirect in vivo imaging support glutamatergic NMDA receptor hypofunction in the disorder. Memantine blocks pathological activation of the NMDA receptors and in this way is protective of the NMDA-producing neuron. Memantine has been demonstrated to result in cognitive improvement in moderate Alzheimer's dementia.

Objective

To assess the effects of memantine on neurocognitive deficits in schizophrenia

Method

The study was a three-month open label trial of memantine at a dose of 20 mg per day. Inclusion criteria included a diagnosis of schizophrenia according to DSM-IV TR with cognitive deficits.

Total number of patients was 18 (male= 11, female= 7). Mean age was 36.8 years (range= 27-54 years). Average duration of illness was 16.7 years. The patients were receiving maintenance treatment which included clozapine, risperidone, olanzapine and quetiapine. Patients were evaluated with the PANSS, Trail Making A & B and WAIS-III at baseline, 2 weeks, 6 weeks and 12 weeks.

Results

Three patients showed significant improvement on the cognitive measures, four patients showed moderate improvement and four patients discontinued memantine due to adverse effects.

Conclusions

Results are of modest clinical significance and indicate that NMDA antagonism may be beneficial in improving cognitive functioning in patients with schizophrenia.

References:

1. 1. Friedman JI. Cholinergic targets for cognitive enhancement in schizophrenia: focus on cholinesterase inhibitors and muscarinic agonists. Psychopharmacology (Berl). 2004 Jun;174(1):45-53. Epub 2004.
2. 4. Bressan RA, Pilowsky LS. Imaging the glutamatergic system in vivo--relevance to schizophrenia, Eur J Nucl Med. 2000 Nov;27(11):1723-31.

NR371 Tuesday, May 23, 12:00 PM - 2:00 PM

Prevalence and Related Factors of Major Depressive and Posttraumatic Stress Disorders Among Health Workers in Golcuk County After the Marmara Earthquake

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize signs that may predict PTSD in health workers.

Summary:

Objective: The prevalences of PTSD and MDD were found to vary between 23-43 % and 16-31 %, respectively in various studies done on the Marmara earthquake victims. Health workers have an increased risk for PTSD and MDD after disasters. The aim of this study was to evaluate the prevalence and predictors of PTSD and MDD among health workers in Golcuk county located in the center of the Marmara Earthquake.

Methods: 98 health workers working in the county enrolled in the study. The participants filled a form which included sociodemographic variables and PTSD-MDD scale. This is a likert type scale which included 23 criteria for PTSD and MDD as well as a subjective assessment of functioning and need for treatment. The answers were coded between 0 and 3 according to distress. SPSS 13.0 program was used in statistical analyses. The results were analysed with descriptive statistics, Mann-Whitney U and chi square tests. P was set at 0.05.

Results: 87.8 % of health workers were females and 92.9 % were married. The prevalances of PTSD and MDD were found to be 9.2 % and 2 % respectively. MDD was seen only in health workers who experienced the earthquake. 88.8 % of those with PTSD experienced the earthquake. The most common PTSD criteria were those of hypervigilance (6.1 %) and lack of future planning (4.1 %). The prevalence of substance abuse was higher in health workers who suffered the earthquake (37.1 %) but this did not reach significance (p=0.064).

Discussion: The prevalences of PTSD and MDD in our sample were found to be similar to previous studies. We could not assess the effect of sex and marital status due to sampling biases. Hypervigilance, lack of planning and substance abuse may predict PTSD and should be recognised in health workers.

References:

1. Palm KM, Polusny MA, Follette VM.Vicarious traumatization: potential hazards and interventions for disaster and trauma workers.1: Prehospital Disaster Med 2004; 19:73-78.
2. Cetin M, Kose S, Ebrinc S, Yigit S, Elhai JD, Basoglu C. Identification and posttraumatic stress disorder symptoms in rescue workers in the Marmara, Turkey, earthquake.1: J Trauma Stress 2005; 18: 485-489.

NR372 Tuesday, May 23, 12:00 PM - 2:00 PM

Pilot Study to Investigate the Effects of a Weight Management Program in Conjunction With Food Provision on Cardiovascular and Endocrine Risk Factors in Patients With Schizophrenia or Schizoaffective Disorder Who Are Treated With Antipsychotic Medications.

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Educational Objectives:

At the conclusion of this presentation the participant should be able to demonstrate a clear understanding of the beneficial effects of the LEARN Program for weight management in conjunction with a food provision strategy for obese patients with schizophrenia or schizoaffective disorder, who are treated with antipsychotic medications. Specifically, the participant should be able to recognize that the intervention will help reduce body weight and improve metabolic parameters and as such reduce cardiovascular and endocrine risk factors.

Summary:

Objective:

We hypothesize that obese patients with schizophrenia or schizoaffective disorder taking antipsychotic medications will show significant and durable weight reduction and improved metabolic profile by participating in the LEARN Program for weight management in conjunction with a food provision strategy.

Method:

Randomised, controlled, prospective study of 18 obese (Body Mass Index $\geq$ 30 kg/m^2) outpatients at the Connecticut Mental Health Center, with schizophrenia or schizoaffective disorder taking typical or atypical antipsychotic medications, comparing body weight, blood pressure, fasting glucose, triglycerides and cholesterol at the begining and end of a 16 week behavioral intervention (LEARN Program plus food provision) or treatment as usual, and then crossed over to the other condition for an additional 16 weeks. All measurements repeated 6 months after completion of intervention.

Results:

For all subjects who completed 6 months (n=12) a significant main effect due to time was observed. There was a decline in the mean weight across time with Mean = 224.0 at week 1, Mean = 217.4 at week 16, and Mean = 213.0 at 6 months, with F (2,20) = 4.78, $p<0.02$, and a significant linear trend ($p < 0.02$) indicating that change happened steadily over time. Pairwise comparisons showed significant weight loss ($p<0.05$) between week 1 and week 16 (Mean = 6.60 lbs) and between week 1 and 6 months (Mean =

10.99 lbs). Paired T tests between week 1 and week 16 for those participants who lost weight showed a significant decline in fasting blood glucose: t(6) = 5.27, p<0.002, two-tailed.

Conclusions:

Health risks of antipsychotic medications can be reduced by a behavioral weight program in conjunction with food provision. These results need to be confirmed in a larger study.

This pilot study was supported by funding from Eli Lilly and Co. and from the Weltner foundation.

References:

1. Allison DB, Mentore JL, Heo M, Chandler LP, Cappelleri JC, Infante MC, Weiden PJ: Antipsychotic induced weight gain: a comprehensive research synthesis. Am J Psychiatry 1999: 156(11): 1986-96.

2. Brownell KD: The LEARN program for weight management. Dallas,TX, American Health Publishing,2000.

NR373 Tuesday, May 23, 12:00 PM - 2:00 PM

Lipid and Glucose Monitoring During Atypical Antipsychotic Treatment: Effects of the 2004 ADA/APA Consensus Statement

Brian Cuffel, Ph.D. *New York, NY*, John Martin, M.P.H., Amie T. Joyce, M.P.H., Stephen J. Boccuzzi, Ph.D., Antony D. Loebel, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant will gain awareness that lipid and glucose monitoring rates in patients receiving atypical antipsychotics is low, despite the publication of consensus recommendations.

Summary:

Objective: In February 2004, the ADA/APA Consensus Development Conference on Antipsychotic Drugs and Obesity and Diabetes here recommended that atypical antipsychotic-treated patients receive routine lipid and glucose monitoring. To assess monitoring rates and the impact of these guidelines, an evaluation of laboratory testing rates before and following guideline publication was performed.

Methods: Patients initiating an atypical antipsychotic before (n=21,848) and after guideline publication (n=8,166) were identified from Pharmetrics' claims database. Lipid and glucose testing was assessed at treatment initiation and 3 months later (as per guidelines).

Results: Lipid and glucose testing rates (6-8% and 16-23%, respectively) were low before and after consensus statement publication. Monitoring rates tended to decline after antipsychotic treatment initiation, before and after guideline publication. Stratification by age did not change the pattern of results.

Conclusions: Based on ADA/APA guideline recommendations, patients undergoing atypical antipsychotic therapy did not receive adequate lipid and glucose monitoring in this large pharmacy claims database analysis. Effective efforts to promote awareness and adherence with monitoring recommendations are needed.

References:

1. Consensus development conference on antipsychotic drugs and obesity and diabetes. J Clin Psychiatry 65 (2); 2004: 267-72.

2. Lieberman et al. Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. N Engl J Med. 2005; 353:1209-1223.

NR374 Tuesday, May 23, 12:00 PM - 2:00 PM

Long-Term Symptomatic Remission in Schizophrenia Patients Treated With Aripiprazole or Haloperidol

John M. Kane, M.D. *Zucker Hillside Hospital, Psychiatry, 75-59 263 Street, Glen Oaks, NY, 11004*, Wim Swyzen, M.D., Xiaoling Wu, Ph.D., Robert McQuade, Ph.D., Rolando Gutierrez-Esteinou, M.D., Quynh Van Tran, Pharm.D., Ronald Marcus, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to discuss the concept and assessment of symptomatic remission in schizophrenia. They will learn the similarities and differences between aripiprazole and haloperidol in long-term maintenance treatment following acute relapse of schizophrenia. They should be aware that although both medications are safe and effective for prevention of relapse in schizophrenia, subjects treated with aripiprazole had greater remission rates, fewer adverse events, and less use of concomitant medication for extrapyramidal symptoms, as demonstrated by an analysis of efficacy data from a placebo-controlled trial.

Summary:

Objective: Assess symptomatic remission rates in patients with schizophrenia receiving aripiprazole or haloperidol in a 52-week, randomized, double-blind, multicenter trial.

Methods: Patients (18-65 years) with acute schizophrenia were randomized to aripiprazole (n = 851) or haloperidol (n = 430) and were treated for 52 weeks. Remission status of randomized patients was evaluated based upon recently developed remission criteria (scores ≤3 on 8 specific PANSS items for ≥6 months). Clinical Global Impression-Improvement (CGI-I) scores, AE-related discontinuation rates, and EPS medication use were also measured.

Results: Significantly more aripiprazole-treated patients satisfied the criteria for symptomatic remission during the trial than those on haloperidol (32% versus 22%; $P < 0.001$). Mean time to achieve PANSS item threshold (~2.9 months) and mean time spent in remission (~9.5 months) were similar for both groups. Those patients achieving remission showed significant improvement on the CGI-I at endpoint compared with non-remitters ($P < 0.0001$ in both groups). Significantly fewer aripiprazole-treated patients discontinued the study due to AEs compared with haloperidol-treated patients (8% versus 18%, respectively, $P < 0.001$). Significantly fewer aripiprazole-treated patients received concomitant EPS medication compared with haloperidol-treated patients (23% versus 57%, respectively; $P < 0.001$).

Conclusions: Over the course of 1 year, significantly more aripiprazole-treated patients with schizophrenia achieved and maintained symptomatic remission as compared with haloperidol-treated patients. Aripiprazole treatment was also associated with significantly fewer discontinuations due to AE-related events and lower concomitant EPS medication use, suggesting that tolerability contributed to the increased remission rate among aripiprazole-treated patients.

References:

1. Andreasen NC, Carpenter WT Jr, Kane JM, et al: Remission in schizophrenia: proposed criteria and rationale for consensus. Am J Psychiatry 2005; 162:441-449.

2. Kasper S, Lerman MN, McQuade RD, et al: Efficacy and safety of aripiprazole vs. haloperidol for long-term maintenance treatment following acute relapse of schizophrenia. Int J Neuropsychopharmacol 2003; 6:325-337.

NR375 Tuesday, May 23, 12:00 PM - 2:00 PM

Patients with Acute Schizophrenia: Treatment With Three Fixed Dosages of Oral Paliperidone Extended-Release Tablets in an International 6-Week Placebo-Controlled Study

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Educational Objectives:

At the conclusion of this session, participants should have an understanding of the efficacy, safety and tolerability of the investigational drug paliperidone extended-release, and the effects on functioning in patients with schizophrenia as assessed using the Personal and Social Performance scale.

Summary:

Objective: This study evaluated the efficacy and tolerability of investigational paliperidone extended-release (paliperidone Extended Release) tablets in patients with acute schizophrenia.

Method: This double-blind, parallel-group, placebo- and active-controlled, dose-response study randomized patients (n=630; age ≥18 years) to receive paliperidone Extended Release 6mg, 9mg, or 12mg, placebo or olanzapine 10mg daily. Olanzapine was included for assay sensitivity only and the study powered to assess the efficacy of paliperidone Extended Release versus placebo.

Results: Mean age=37.1y±10.9. Mean PANSS total score (93.9±11.0 in the intention-to-treat population [n=628] at baseline) improved at endpoint for paliperidone Extended Release versus placebo (6mg=-17.9±22.2, 9mg=-17.2±20.2, 12mg=-23.3±20.1, placebo=-4.1±23.2; p<0.001; [olanzapine change=-19.9±19.0]). Patient functioning was assessed using the Personal and Social Performance Scale: scores improved at endpoint for paliperidone Extended Release versus placebo (6mg=9.1±15.5, 9mg= 8.1±14.5, 12mg=11.5±16.0, placebo=0.5±15.5; p<0.001). Treatment-emergent adverse avents (TEAEs) occurring >3% more than with placebo were tachycardia, extrapyramidal disorder and hyperkinesia (paliperidone Extended Release) and somnolence, tachycardia and postural hypotension (olanzapine). TEAE-EPS were comparable for paliperidone Extended Release 6mg, olanzapine and placebo, but increased with paliperidone Extended Release 9mg and 12mg. Serious AE frequency was similar among paliperidone Extended Release (3%), olanzapine (2%) and placebo (2%).

Conclusions: In this study, paliperidone Extended Release 6mg, 9mg and 12mg was effective, well tolerated and associated with functional improvements in the treatment of schizophrenia.

References:

1. Falkai P, Wobrock T, Lieberman J, et al.: World Federation of Societies of Biological Psychiatry (WFSBP) guidelines for biological treatment of schizophrenia, Part 1: acute treatment of schizophrenia. World J Biol Psychiatry 2005; 6(3):132-191.
2. Practice guidelines for the treatment of patients with schizophrenia (2nd Edition), February 2004. Available at: http://www.psych.org/psych_pract/treatg/pg/Practice20Guidelines8904/Schizophrenia_2e.pdf.

NR376 Tuesday, May 23, 12:00 PM - 2:00 PM

Suicidality in Schizophrenia as a Separate Symptom Domain That may be Independent of Depression or Psychosis

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that suicidality in chronic schizophrenia was associated with hopelessness, and it might also be independent from other symptom dimensions of schizophrenia.

Summary:

Background: Suicide is the leading cause of premature death among patients with schizophrenia. Among risk factors, previous suicide attempts and hopelessness appear to be the most important risk factors. Meanwhile, suicidality is suggested to represent a separate symptom domain that is related to, but independent of, depression or psychosis. The author explored the relationship between suicidality and depressive and psychotic symptoms in schizophrenia. Methods: Data from a previous study were utilized, and the subjects consisted of 59 inpatients with a DSM-IV diagnosis of chronic schizophrenia or schizoaffective disorder. Among the patients, 27 (46%) were women; the patients had a mean age of 47.1 (SD=11.5), and a mean age at onset of 28.7 years (9.1). Assessments were performed using the Calgary Depression Scale for Schizophrenia (CDSS) for suicidality and hopelessness and the 18-item Brief Psychiatric Rating Scale (BPRS, 0-3 score: 0= none, 1=mild, 2=moderate, 3=severe) for psychotic symptoms. Results: First, a principal component factor analysis with varimax-rotation was applied to the complete items set of the BPRS with two items (hopelessness and suicide) of the CDSS. The factor analysis revealed seven symptom dimensions (factors) with Eigenvalues over 1.0: Positive, Hostile, Negative, Anxious/Depressive (AD), Suicidal, Cognitive, and Stereo-typed factors (data available upon request). Hopelessness and suicide items loaded on the same factor, but failed to load on any one of the other six obtained factors. Second, hopelessness, but not positive, negative, or even the AD psychopathology factor scores was associated with suicidality. Third, a multiple regression analysis with step-wise forward selection was used to predict suicidality from hopelessness, positive, negative, and AD psychopathology factor scores. The regression models predicting suicidality indicated only hopelessness to be a significant predictor. Conclusions: These findings suggested suicidality to be associated with hopelessness in chronic schizophrenia, and it might also be independent from other symptom dimensions of schizophrenia.

References:

1. Lindenmayer JP, Czobor P, Alphs L, Nathan AM, Anand R, Islam Z, Chou JC: The InterSePT scale for suicidal thinking reliability and validity. Schizophr Res 2003; 63:161-170.
2. Meltzer HY: Treatment of suicidality in schizophrenia. Ann NY Acad Sci 2001; 932:44-58.

NR377 Tuesday, May 23, 12:00 PM - 2:00 PM

The Effects of Olanzapine, Quetiapine, and Risperidone on Neurocognitive Function in First-Episode Psychosis: A Double-Blind, 52-Week Comparison

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Educational Objectives:

At the conclusion of this presentation, the participant should have gained knowledge of: 1) the neurocognitive measures used in the study; and 2) the similarities and differences between olanzapine, quetiapine, and risperidone in their effects on neurocognitive function in first-episode patients with psychosis.

Summary:

Objective: To compare the effects of olanzapine, quetiapine, and risperidone on neurocognitive function in patients experiencing a first psychotic episode.

Methods: A 52-week, randomized, double-blind, multicenter study of first-episode patients randomized to olanzapine (2.5 to 20 mg/day), quetiapine (100 to 800 mg/day), or risperidone (0.5 to 4 mg/day). Patients completed neurocognitive assessments at baseline, 12, and 52 weeks. Neurocognitive composite scores were calculated from a battery of tests developed for the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) schizophrenia clinical trial and the Brief Assessment of Cognition in Schizophrenia (BACS).

Results: The mean (SD) modal prescribed daily dose (mg) of olanzapine, quetiapine, and risperidone in the 400 randomized patients was 11.7 (5.3), 506 (215), and 2.4 (1.0), respectively. At Week 12, there was significant improvement in cognition for each treatment ($p<0.01$), with mean composite Z-score improvements of 0.18 for olanzapine, 0.34 for quetiapine, and 0.27 for risperidone. There was no significant overall difference between treatments. Quetiapine improved cognition more than olanzapine and risperidone on five and four of the 15 individual measures at 12 weeks ($p<0.05$), respectively. Risperidone improved cognition more than olanzapine at 12 weeks on one measure ($p<0.05$). At Week 52, statistically significant relationships emerged between neurocognitive composite scores and functional outcome for olanzapine and quetiapine.

Conclusions: Olanzapine, quetiapine, and risperidone significantly improved neurocognitive function in patients with first-episode psychosis, and these improvements were related to changes in functional outcome. While overall composite scores did not differentiate treatments, quetiapine was associated with greater improvement on several individual measures.

The CAFE research program was coordinated by the University of North Carolina. Funding for this academic center was provided by AstraZeneca Pharmaceuticals LP.

References:

1. Harvey PD, Keefe RS. Studies of cognitive change in patients with schizophrenia following novel antipsychotic treatment. Am J Psychiatry 2001;158(2):176-84.
2. Keefe RS, et al. Neurocognitive assessment in the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) project schizophrenia trial: development, methodology, and rationale. Schizophr Bull 2003;29(1):45-55.

NR378 Tuesday, May 23, 12:00 PM - 2:00 PM

Utilization Patterns of Olanzapine and Risperidone at a VA Medical Center

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Educational Objectives:

At the conclusion of the presentation, participants will demonstrate knowledge of the elements required in conducting medication utilization studies. They will also recognize the impact of different factors on utilization patterns of the two most commonly prescribed antipsychotic medications in a large system of care.

Summary:

Objective: To compare the utilization of the two most commonly prescribed antipsychotic medications, olanzapine (Olanzapine®) and risperidone (Risperidone®), at our Veterans Administration (VA) medical center. We also aimed to assess the impact of a concurrent VA system recommendation to use risperidone (Risperidone®) as first line agent on utilization.

Method: Using electronic database, we extracted all olanzapine (Olanzapine®) and risperidone (Risperidone®) outpatient prescriptions January 1999-December 2000 and calculated the supply in days for each prescription. We compared discontinuation rates due to a switch between the two medications or a gap of > 30 days in medication supply. The first medication trial in the study period was designated as the "index" trial. We also obtained diagnostic and demographic information.

Results: Sample included 2160 patients. Only 51% were diagnosed with schizophrenia. For index trials, schizophrenia patients were more likely to switch (OR= 1.9, 95% CI: 1.4-2.5, $p< 0.001$) and to have a gap (OR= 1.7, 95% CI: 1.4-2.1, $p< 0.001$), but maintained a longer trial duration (B= 62, 95% CI: 47-76, $p<0.001$). Schizophrenia patients on olanzapine (Olanzapine®) were less likely to switch, but more likely to have a gap. Guidelines recommending risperidone (Risperidone®) as first line agent increased its initiation rate (60%), less so in schizophrenia (55%), where the difference dissipated (49%) upon the first medication switch in new adequate trials.

Conclusion: Olanzapine (Olanzapine®) and risperidone (Risperidone®) are commonly prescribed for non-schizophrenia patients. Schizophrenia diagnosis best predicted utilization. System guidelines favoring a first line agent are unlikely to have a significant impact on utilization in complex diseases such as schizophrenia necessitating alternative approaches.

References:

1. Sernyak MJ. Rosenheck R: Risk Adjustment in Studies Using Administrative Data. Schizophr Bull 2003; 29:267-271.
2. Douglas LL, Rosenheck RA: From Conventional to Atypical Antipsychotics and Back: Dynamic Processes in the Diffusion of New Medications. Am J Psychiatry 2002; 159:1534-1540.

NR379 Tuesday, May 23, 12:00 PM - 2:00 PM

Prognostic Factors in Postpsychotic Depression of Schizophrenia

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Educational Objectives:

Undertanding of the postpsychotic depression of schizophrenia

Summary:

This study was conducted to investigate the prognostic factor in postpsychotic depression of schizophrenia. The 80 patient selected using the diagnosis based DSM-IV, PANSS and ESRS. Each patents was surveyed about demographic and clinical characteristics, and then the subjective depressive symptom and objective depressive symptoms, and insight of psychosis were evaluated. The subjective depressive symptoms were evaluated by BDI and ZDS, objective depressive symptoms were evaluated by HDRS and CDSS, and insight of psychosis was evaluated by KISP. The comparisons using demographic and clinical characteristics were reveal that HDRS and CDSS had significant difference at sex and suicide attempts, BDI at education level and onset age. The patients having above cuff-off score at each scale were 20(25.0%) in BDI, 16(20.0%) in ZDS, 18(22.5%) in CDSS and 6(7.5%) in HDRS. The result of stepwise multiple regression analysis revealed that the score of KISP, education level, sex and suicide attempts were main prognostic factor in psychotic depressive disorder of schizophrenia. The main prognostic factor in psychotic depressive disorder of schizophrenia was the insight of psychosis, suicidal attempts, etc. Especially the insight of psycho-

sis was most liable prognostic factors but negativistic relationship with depressive symptoms.

References:

1. Addington DD, Azorin JM, Falloon IRH, Gerlach J, Hirsch SR, Siris SG. Clinical issues related to depression in schizophrenia: an international survey of psychiatrists. Acta Psychiatr Scand 2002;105:189-95.

2. Sirls SG, Adan F, cohen M, Mandeli J, Aronson A, Ca-sey E: Postpsychotic depression and negative symptoms : An investigation of symdromal overlap. Am J psychiatry 1988;145:1532-7.

NR380 Tuesday, May 23, 12:00 PM - 2:00 PM

Association of Attitude Towards Medication With Neurocognitive Function in Schizophrenia

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Educational Objectives:

Participants will acknowledge that maintaining the positive attitude toward medication is associated with neurocognitive function in patients with schizophrenia.

Summary:

Introduction: Attitude toward medication is important for medication adherence which is a key determinant of outcome in schizophrenia. This study aimed to establish the relationship between attitudes towards medication and neurocognitive function in schizophrenia patients.

Method: Sixty-two patients meeting the DSM-IV criteria for schizophrenia participated in this study. The attitude of the subjects towards medication were evaluated by Drug Attitude Inventory (DAI) and followed up at 12-weeks. Neurocognitive function was evaluated using the following computerized battery: Digit Span, Verbal Learning Test (VLT), CPT, Wisconsin Card Sorting Test (WCST), Finger Tapping Test, Trail Making Test A and B, and Mini-mental Status Examination (MMSE). Follow-up ratings on the same clinical ratings including attitude toward medication and neurocogntive function were subsequently obtained after 12 weeks of the baseline assessment. The association of attitude toward medication with neurocognitive function and clinical characteristics was analyzed in a cross-sectional, prospective manner.

Results: The scores on DAI were significantly correlated with measures on the VLT, WCST, and CPT. Subjects with positive attitudes towards medication performed significantly better than those with negative attitudes on the WCST. The performances on the WCST, VLT, and MMSE were significantly better in the subjects who had positive attitudes towards medication at the index evaluation and maintained them until the follow-up evaluation than in those who had negative attitudes or failed to maintain positive attitudes toward medication.

Conclusion: Our findings support an association between positive attitudes towards medication and neurocognitive function. In particular, maintaining a positive attitude toward treatment for a long period was associated with better executive function and verbal learning memory.

References:

1. Goodman C, Knoll G, Isakov V, Silver H: Negative attitude towards medication is associated with working memory impairment in schizophrenia patients. Int Clin Psychopharmacol 2005; 20:93'96.

2. Jeste SD, Patterson TL, Palmer BW, Dolder CR, Goldman S, Jeste DV. Cognitive predictors of medication adherence among middle-aged and older outpatients with schizophrenia. Schizophr Res 2003; 63: 49'58.

NR381 Tuesday, May 23, 12:00 PM - 2:00 PM

Symptom Worsening Associated With Treatment Discontinuation in Schizophrenia Trials

Bruce J. Kinon, M.D. *Eli Lilly and Company, Lilly Corporate Center, DC4133, Indianapolis, IN, 46285*, Haya Ascher-Svanum, Ph.D., Lei Chen, M.S., Hassan Jamal, M.S.C., Glenn A. Phillips, Ph.D.

Educational Objectives:

To get a better understanding of the relationship between schizophrenia treatment discontinuation and symptom improvement as measured by PANSS.

Summary:

Introduction: Treatment discontinuation, common in antipsychotic trials for the treatment of schizophrenia, may be associated with symptom worsening

Methods: Data from 4 randomized, double-blind studies (n= 1627; 24-28 weeks duration) were used in this pooled post-hoc analysis. Patients with schizophrenia or a related disorder were treated with olanzapine (n=822), risperidone (n=167), quetiapine (n=175), or ziprasidone (n=463). Changes in PANSS total scores (PTS) were analyzed by ANOVA, while generalized estimating equations (GEE) were used to model discontinuation status versus concurrent PTS changes.

Results: A total of 865 (53%) patients discontinued treatment over the entire study. Mean PTS decreased from 91 to 71 during the study (LOCF; completers from 91 to 59; discontinuers from 91 to 85). Early in treatment (Weeks 0-4), discontinuers had no significant change in mean PTS from their previous visit, and 21% of discontinuers (versus 61% of completers) achieved clinical response, defined as 20% or more PTS reduction from baseline. Overall, discontinuers had symptom worsening or less improvement on PTS in a given interval. Similarly, individuals who discontinued due to adverse events experienced symptom worsening, or insignificant decreases in PTS compared to their previous visit. Overall, there was a 70% estimated increase in odds for discontinuation for every 10-point PTS increase, within any given visit interval.

Conclusions: Findings from post-hoc analyses of a large pooled sample of patients suggest that failure to establish early treatment response, as well as recent loss of previous symptom improvement, may lead to treatment interruption and discontinuation.

References:

1. Nose M, Barbui C, Tansella M: How often do patients with psychosis fail to adhere to treatment programmes? A systematic review. Psychol Med 2003, 33:1149-1160.

2. Perkins DO: Predictors of noncompliance in patients with schizophrenia. J Clin Psychiatry 2002, 63:1121-1128.

NR382 Tuesday, May 23, 12:00 PM - 2:00 PM

Characteristics of Involuntarily Admitted Psychiatric Patients. A Case-Control Study of 30 Inpatients With Psychotic Symptoms.

Rémy Klein *CHU Casselardit, kleinremy@free.fr, Toulouse, 31300, France*, Lionel Cailhol, Eric Bui, Laurent J. Schmitt, Philippe J.R. Birmes

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize caracteristics of committed inpatients

Summary:

Background and Objective: Involuntary psychiatric admissions have been increasing in France for fifteen years. However, effects of coercion on clinical evolution is not fully understood. This study aims at exploring socio-demographic and clinical characteristics of involuntarily committed patients with psychotic symptoms.

Methods: During 2 months, we enrolled 30 continuous subjects aged under 65 and admitted for psychotic symptoms to a psychiatric ward of an University Hospital. Ten days after admission, we assessed each participant with the Mini International Neuropsychiatric Interview, the Brief Psychiatric Rating Scale, the 30-item Nurses Observation Scale for Inpatient Evaluation for symptoms intensity, the Scale to assess Unawareness of Mental Disorder, and the Barrier Treatment Inventory, an experimental questionnaire assessing cognitive representations of disease and care. Using different correlation tests, we analysed the associations between coercion and each socio-demographic and clinical characteristic.

Results: 17 inpatients were involuntarily committed (56%). Mean age was 35.4 (SD=10.5), and 17 participants (56%) were female. Involuntary admission was significantly associated with history of major depressive episode and poorer insight of awarness of treatment effectiveness and delusional symptoms. The analysis failed to show any significant differences between the two groups in terms of socio-demographic characteristics and symptoms severity.

Conclusion: This study underlines the high prevalence of negative representations of care in involuntary commitment.

References:

1. Kelly BD: Clinical predictors of admission status in first episode schizophrenia. European Psychiatry 2003; 19: 67-71.
2. Crisanti AS: characteristics of psychiatric inpatients detained under civil commitment legislation : a canadian study. International Journal of Law and Psychiatry 2001; 24: 399-410.

NR383 Tuesday, May 23, 12:00 PM - 2:00 PM

Anticipatory Stress in the Population Facing Removal From the Gaza Strip

Robert Kohn, M.D. *Brown University, Psychiatry and Human Behavior, 345 Blackstone Boulevard, Providence, RI, 02906*, Miriam Billig, Ph.D., Itzhak Levav, M.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to understand the role of population removal on psychological distress and understand the impact of prior life events, such as terrorism on a current life event.

Summary:

Background: The government of Israel decided in March 2005 to remove the Israeli population settled in the Gaza Strip, a process known as "disengagement". The goal of this study is to assess emotional distress, measured by the D-PERI, among adult settlers residing in the Gaza Strip a few months before their scheduled removal and during a period of resistance mobilization.

Methods: One person per household in 13 recognized settlements (n = 267) were randomly selected for a telephone interview that included the D-PERI. Regression analysis was used to determine the best predictive model for demoralization, as well as current self-appraisal. Additionally, the D-PERI scores were compared with other historical population controls in Israel.

Results: Being female, less years of education, higher anxiety provocation, greater alienation, worse religious coping, poorer perceived health, having no family outside the occupied territories, and living in a secular settlement increased the risk of being demoralized. Positive current self-appraisal was associated with greater attachment, less anxiety provocation, more ideological position, less feelings of alienation, a more positive view of the future, and plans to return to Gaza.

Conclusions: Prior exposure to terrorism possibly has attenuated the degree of distress in the population being displaced from Gaza

References:

1. Heller T: The effects of involuntary residential relocation: a review. Am J Community Psychol 1982; 10:471-492.
2. Steinglass P, Kaplan De-Nour A, Shye S: Factors influencing psychosocial adjustment to forced geographical relocation: the Israeli withdrawal from the Sinai. Am J Orthopsychiatry 1985; 55: 513-529.

NR384 Tuesday, May 23, 12:00 PM - 2:00 PM

Treatment Discontinuation in Antipsychotic Trials and Change in Schizophrenia Symptoms

Sara Kollack-Walker, Ph.D. *Eli Lilly and Company, Lilly Corporate Center, DC4133, Indianapolis, IN, 46285*, Adam Meyers, M.S., David Adams, Ph.D., Haya Ascher-Svanum, Ph.D., Bruce J. Kinon, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to discuss reasons for antipsychotic treatment discontinuation in clinical trials and the association between improvement in specific symptom domains and treatment discontinuation.

Summary:

Objective: To examine the association between treatment discontinuation in antipsychotic trials and change in schizophrenia symptoms.

Methods: A post hoc, pooled analysis of 4 randomized, 24-28 week, double-blind, head-to-head trials of atypical antipsychotics for treatment of schizophrenia spectrum disorders (N=1627) compared trial completers with non-completers on improvements in positive, negative, and depressive symptoms, measured by the Positive and Negative Syndrome Scale. Symptom severity and change were used to predict trial discontinuation.

Results: Fifty-three percent (866/1627) of patients discontinued early. Poor response or symptom worsening was the most frequent reason for discontinuation (36%; 315/866). Non-completers showed significantly less depressive, positive, and negative symptom improvement compared with completers. Patients with less severe baseline depressive symptoms (hazard ratio [HR]=0.95; 95% Confidence Interval [CI] 0.93, 0.97; p<.001) and positive symptoms (HR=0.97; 95% CI 0.95, 0.98; p<.001) were less likely to discontinue. Patients with improvements in depressive symptoms (HR= 0.94 for a unit-point change; 95% CI 0.92, 0.96; p<.001) and positive symptoms (HR=0.95; 95% CI 0.93, 0.96; p<.001) were less likely to discontinue at a subsequent visit independent of baseline severity. A 20% improvement in depressive and positive symptoms in the first 2 weeks was associated with a 50% (odds ratio [OR]=1.52; 95% CI 1.22, 1.90) and 70% (OR=1.71; 95% CI 1.35, 2.16) greater likelihood of completion, respectively. Baseline or change in negative symptoms did not significantly predict discontinuation.

Conclusions: Poor response or symptom worsening was the most frequent reason for treatment discontinuation. In particular, poor improvement of depressive and positive symptoms predicted treatment discontinuation.

References:

1. Lieberman JA, Stroup TS, McEvoy JP, et al. Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. The New England Journal of Medicine 2005; 353:1209-1223.
2. Dunayevich E, Zhao F, Ascher-Svanum H, Mitchell CP, Phillips GA, Dellva MA, Green A. Increased time to all-cause antipsychotic trial discontinuation is associated with better schizophrenia treatment outcomes. Abstract. Biol Psychiatry 2005;57;107.

NR385 Tuesday, May 23, 12:00 PM - 2:00 PM

Characterizing the Stages of Schizophrenia

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Educational Objectives:

At the conclusion of this presentation, the participant should recognize the importance of staging in schizophrenia and be able to identify distinctions in symptoms, function, and clinical status among the stages of this illness.

Summary:

Background: Although diagnostic criteria exist for schizophrenia, the disease course is less well defined. A prior initial analysis of the various stages of schizophrenia (acute, stable, and remitted) suggested symptom profiles may be characteristic and definable for each of the stages. We expand on those findings, examining measures of insight, functioning, and overall status in stable and remitted populations to guide further characterization of these stages.

Methods: Data are from a post-hoc analysis of a 1-year study in stable patients with schizophrenia. Remitted patients were identified by recently defined criteria (Andreasen et al 2005). Measures included the Strauss-Carpenter Levels of Functioning (LOF), the Personal and Social Performance Scale (PSP), Positive and Negative Syndrome Scale (PANSS), and Clinical Global Impressions (CGI) scale.

Results: Clinical observation of data from stable and remitted patients showed differences in most LOF items, with overall higher mean scores in the remitted group. Notable differences existed in measures of social functioning, quality/quantity of work, and overall level of functioning. The percentage of patients with good functioning (PSP total = 71-100) was 27.6% in stable patients and 40.5% in remitters. Mean (±SD) insight scores (PANSS item G12) were 2.5 ± 1.3 in stable patients and 2.1 ± 0.87 in remitted patients . Mean CGI scores reflected mild-moderate illness in stable patients and borderline-mild illness in remitted patients.

Conclusions: These data provide information to guide the characterization of the stages of schizophrenia. In addition to distinct symptom profiles, results show how measures of functioning, insight, and clinical status may contribute to defining these stages. Future efforts will consider measures of cognition, stress tolerance, and physical health. Crucial issues relevant to various stage transitions will be explored.

Sponsored by Janssen, LP.

References:

1. Andreasen NC, Carpenter W, Kane JM, Lasser RA, Marder SR, Weinberger DR. Remission in schizophrenia: proposed criteria and rationale for consensus. Am J Psychiatry 2005; 162:441-449.
2. Simpson G, Lasser RA, Bossie CA, Rodriguez S, Turkoz I, Gharabawi G. Maintenance of effect with long-acting risperidone: A one-year double-blind comparison of two doses in patients with schizophrenia or schizoaffective disorder. J Clin Psych. In prep.

NR386 Tuesday, May 23, 12:00 PM - 2:00 PM

Healthcare Resource Utilization Pre/Post Risperidone Long-Acting, Injectable Treatment Initiation in a Managed Care Population

Chris Kozma, Ph.D. *University of South Carolina, Independent Consultant and Adjunct Professor, 112 Fox Hollow Circle, West Columbia, SC, 29170*, Sarah Poston, Pharm.D., Julie Locklear, Pharm.D.

Educational Objectives:

To assess healthcare utilization and associated cost in schizophrenia and schizoaffective patients pre/post risperidone long-acting injectable (RLAI; Risperdal® CONSTA®) treatment initiation.

Summary:

Objective:

To assess healthcare utilization and associated cost in schizophrenia and schizoaffective patients pre/post risperidone long-acting injectable (RLAI; Risperidone® CONSTA®) treatment initiation.

Methods:

A retrospective evaluation utilized pharmacy and medical claims to assess healthcare resource utilization and costs of adult patients with schizophrenia using a mental-health subset of managed-care data. Inclusion criteria required diagnosis of schizophrenia or schizoaffective disorder, at least 1 claim for RLAI between December 2003 and June 2004, and 6 months' continuous eligibility criteria before and after the initial RLAI claim, which served as the index date. The observation period was 12 months, including 6 months pre- and 6 months post-RLAI treatment initiation, where patients served as their own control. Healthcare utilization outcome variables included hospitalizations, emergency-room use, outpatient visits, and medications. Costs represent the amount paid by the health plan for services.

Results:

Results are available for 26 patients meeting inclusion criteria. Mean (±SD) patient age was 37 ± 13.4 years, and 53.8% were male. The mean number of hospitalizations per patient decreased from 0.77 in the pre-period to 0.35 in the post-period ($P = 0.06$). Mean hospitalizations costs (±SD) decreased from $14,456 ± $28,745 in the pre-period to $4,201 ± $13,876 ($P < 0.05$). Outpatient utilization remained statistically unchanged between the pre- and post-period, while the costs for psychoactive medications significantly increased in the post period. Total healthcare costs (±SD) trended downward, from an average of $22,650 ± $30,856 in the pre-period to $15,182 ± $18,209 in the post-period ($P = 0.09$). Sensitivity analyses conducted around the index date resulted in a statistically significant decrease in total healthcare costs in the post period.

Conclusions:

In this US managed-care patient population, hospitalization costs significantly decreased post (RLAI) treatment initiation. Further studies with larger sample sizes are needed to confirm findings.

Funding source: Ortho-McNeil Janssen Scientific Affairs, LLC

References:

1. Kane JM, Eerdekens M, Lindenmayer JP, Keith SJ, Lesem M, Karcher K: Long-acting injectable risperidone: efficacy and safety of the first long-acting atypical antipsychotic. Am J Psychiatry 2003; 160:1125-1132.
2. Eriksson L et al.: Presented at the 42nd Annual Meeting of The American College of Neuropsychopharmacology, December 7-11, 2003, San Juan, Puerto Rico.

NR387 Tuesday, May 23, 12:00 PM - 2:00 PM

A Double-Blind, Placebo-Controlled Study of Olanzapine in Adolescents With Schizophrenia

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to decide upon the appropriateness of treating adolescent patients with schizophrenia with olanzapine.

Summary:

Objective: Data from an olanzapine double-blind, placebo-controlled trial are presented.

Methods: Adolescents (13-17 years) with schizophrenia received flexible doses of olanzapine (2.5-20mg/day) or placebo for six weeks. LOCF mean changes from baseline-to-endpoint were assessed from the BPRS-C and CGI-S. Response was defined as a ≥30% decrease in BPRS-C and a CGI Severity ≤3.

Results: One-hundred-seven adolescents with schizophrenia (olanzapine n=72, age=16.1±1.3; placebo n=35, age=16.3±1.6) were randomized (2:1). The mean dose of olanzapine was 11.1±4.0mg/day. Olanzapine-treated patients experienced significant improvements compared with placebo in BPRS-C (p=.003) and CGI-S (p=.004). The treatment response rate was not significantly different between olanzapine- (37.5%) and placebo-treated patients (25.7%). Treatment-emergent adverse events occurring significantly more often in olanzapine-treated patients included increased weight and somnolence. Olanzapine-treated patients gained significantly more weight (4.3±3.3kg versus 0.1±2.8kg, p<.001). Significantly more olanzapine-treated patients experienced treatment-emergent high AST/SGOT, ALT/SGPT, prolactin; low bilirubin, hematocrit at any time during treatment. There was a significant increase at endpoint in fasting triglycerides (p= .029) in olanzapine-treated patients. **Conclusions:** In adolescents, olanzapine compared with placebo treatment led to significant improvements on several efficacy measures.

References:

1. Kumra S, Frazier JA, Jacobsen LK, McKenna K, Gordon CT, Lenane MC, Hamburger SD, Smith AK, Albus KE, Alaghband-Rad J, Rapoport JL: Childhood-onset schizophrenia. A double-blind clozapine-haloperidol comparison. Arch.Gen.Psychiatry 1996; 53:1090-1097.
2. Spencer EK, Kafantaris V, Padron-Gayol MV, Rosenberg CR, Campbell M: Haloperidol in schizophrenic children: early findings from a study in progress. Psychopharmacol.Bull. 1992; 28:183-186.

NR388 Tuesday, May 23, 12:00 PM - 2:00 PM

Atypical Antipsychotics and the Risk OF Developing Diabetes

Jaime Caro *Boston, MA*, Alex Ward, Annette Lam, Proskorovsky Irina, Khajak J. Ishak

Educational Objectives:

To evaluate the risk of developing diabetes among patients treated with olanzapine, quetiapine or risperidone.

Summary:

Objective: To evaluate the risk of developing diabetes among patients treated with olanzapine, quetiapine or risperidone. **Methods:** Using the Quebec Prescription Drug Insurance Plan database, 110,243 patients with at least 1 prescription for olanzapine (n=38,637), quetiapine (n=23,624), or risperidone (n=47,982) between July 1, 2000, and December 31, 2004, with no pre-existing diabetes or clozapine use were studied. Hazards of new diabetes (defined as ICD-9 250 diagnosis on admission to hospital or by primary care physician, or prescription for insulin or oral hypoglycemic agent) were analyzed. Proportional hazard analyses were used to control for age, gender and schizophrenia. **Results:** Unadjusted hazard ratio versus risperidone were 1.09 (95% CI=1.02-1.17) for olanzapine and 1.07 (95% CI=0.99-1.17) for quetiapine. Adjusting for age, gender, and schizophrenia diagnosis increased the ratios to 1.11 (95% CI=1.04-1.18, p=0.0027) and 1.16 (95% CI=1.07-1.26, p= 0.0006). **Conclusions:** The continued finding of elevated risks of diabetes with some atypicals is worrisome given heightened awareness of this association.

References:

1. Caro JJ, Ward A, Levinton C, Robinson K. The risk of diabetes during olanzapine use compared with risperidone use: a retrospective database analysis. J Clin Psychiatry 2002; 63: 1135-9.
2. Moisan J, Grégoire J-P, Gaudet M, Cooper D. Exploring the risk of diabetes mellitus and dyslipidemia among ambulatory users of atypical antipsychotics: a population-based comparison of risperidone and olanzapine. Pharmacoepi Drug Saf 2005; 14: 427-36.

NR389 Tuesday, May 23, 12:00 PM - 2:00 PM

Identifying Predictors of Remission in Patients With Schizophrenia

Robert Lasser, M.D. *Johnson & Johnson Pharmaceutical Services, LLC, 700 US Highway 202 South, Raritan, NJ, 08869*, Georges Gharabawi, M.D., Cynthia Bossie, Ph.D., Ibrahim Turkoz, M.S., Mary Kujawa, M.D., Judith Kando, Pharm.D., Henry Nasrallah, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the correlation between a number of different patient variables and the expectation for achieving remission in patients with schizophrenia.

Summary:

Objective: Recently, increased attention has been given to the concept of achieving remission in patients with schizophrenia. This analysis explored predictors of remission in stable patients with schizophrenia or schizoaffective disorder.

Methods: Subjects who met criteria for remission (Andreasen et al. 2005) in a 1-year study of long-acting risperidone 25 or 50 mg every 2 weeks, were examined in a post-hoc analysis. Correlation analyses explored the relationship between meeting remission criteria and demographic and clinical patient variables (including baseline scores on the Positive and Negative Syndrome Scale [PANSS], Personal and Social Performance Scale [PSP], Strauss-Carpenter Levels of Functioning [LOF], and a cognitive battery). A stepwise multivariate logistic model identified predictors of remission.

Results: Data show significant, albeit weak, correlations between meeting remission criteria and baseline scores on the PANSS disorganized-thought factor (Pearson coefficient = -0.20, P <0.001), insight (-0.14, P = 0.0121), and PSP total score (0.24, P<0.001). Significant correlations were found with baseline scores on LOF items (including overall functioning, item 7), and 3 of 7 cognitive domains (visual memory, working memory, social cognition). The multivariate logistic model identified significant baseline predictors of remission as: (1) sex (OR = 0.51, P =0.0500), suggesting a 49% reduction in the odds of remission in males versus females; (2) PANSS disorganized-thought factor score (OR = 0.90, P = 0.0112), suggesting 10% decreased odds of remission per unit increase in the factor score; (3) LOF item 7 (OR = 1.65, P =

0.0180), indicating 65% increased odds of remission with each unit increase in LOF item 7; and (4) visual-memory cognitive domain (OR = 1.51, $P = 0.0314$), suggesting patients are 1.5 times more likely to remit per unit increase in the visual-motor Z-score.

Conclusions: These data show that distinct patient variables may be predictors of achieving remission.

Supported by Janssen, LP.

References:

1. Andreasen NC, Carpenter WT Jr, Kane JM, Lasser RA, Marder SR, Weinberger DR: Remission in schizophrenia: proposed criteria and rationale for consensus. Am J Psychiatry 2005; 162:441-449.

2. Rodriguez S, Lasser R; Turkoz I, Gharabawi G, Chung H, Simpson G: A 52-week randomized trial of long-acting risperidone maintenance therapy in schizophrenia. Poster presented at: the 45th Annual NCDEU Meeting; June 6-9, 2005; Boca Raton, Fla.

NR390 Tuesday, May 23, 12:00 PM - 2:00 PM

Reduced Risk of Cancer Among Parents and Siblings of Patients With Schizophrenia

Itzhak Levav, M.D. *Ministry of Health, Israel, 29 Rivka, Jerusalem, 93461, Israel*, Robert Kohn, M.D., Irena Lipshitz, M.A., Micha Barchana, M.D., Ilya Nobikov, Ph.D., Alexander Grinshpoon, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand the relationship of developing cancer among those with schizophrenia, their siblings, and parents.

Summary:

Objectives: Studies have shown that the risk for cancer is lower among persons with schizophrenia. Of the hypotheses raised to explain such a finding, the genetic basis received repeated support. If this were the case, the risk among first-degree relatives would show an equal reduced risk. However, two prior studies arrived at contrasting results, low risk and no difference. To investigate the risk for cancer among biological parents and full siblings (with and without schizophrenia) of persons hospitalized for schizophrenia.

Methods: The national psychiatric and cancer case registers enabled the replication of the above studies and addressed confounding factors that were imputed for the discrepant results. Linkage analysis was conducted between three databases, population, psychiatric and cancer registers. The index cases were born in Israel or that immigrated by age 5 and had received the diagnosis of schizophrenia upon discharge during their last psychiatric inpatient hospitalization.

Main outcome measures: Standard incident ratios (SIRs) were calculated by gender based on the comparison of the age-specific incidence rates for all types of cancer among the first-degree relatives of persons hospitalized with schizophrenia with similar incidence measures in the general population.

Results: There was a consistent risk reduction across all groups, index cases, parents and siblings. The SIR among mothers and fathers excluding those with schizophrenia reached statistical significance in contrast to the general population, 0.83 (95% CI 0.76-.0.90) and 0.87 (95%CI 0.79-.095), respectively. There was an analogous significant reduction for sisters SIR, 0.72 (95% CI 0.58-0.88). The respective reduction for brothers and for female and male index cases (0.92, 0.66 and 0.89) did not reach significance, likely, because of reduced statistical power.

Conclusions: The genetic hypothesis, eg, the presence of a gene with a dual effect, reduction of cancer risk through apoptosis and disruption of neurodevelopment, received support in this study.

References:

1. Grinshpoon A, Barchana M, Ponizovsky A, Lipshitz I, Nahon D, Tal O. Weizman A, Levav I. Cancer in schizophrenia: Is the risk higher or lower. Schiz Res 2005; 333-341.

2. Dalton SO, Laursen TL, Mellemkjaer L, Johansen C, Mortensen PB. Risk of cancer in parents of patients with schizophrenia. Am J Psychiatry. 2004; 161: 903-908.

NR391 Tuesday, May 23, 12:00 PM - 2:00 PM

Metabolic Effects of Aripiprazole Versus Standard of Care (The STAR Trial)

Gilbert L'Italien, Ph.D. *Bristol Meyrs Squibb, 5 research parway, Wallingford, CT 06492, CT*, Linda Hanssens, M.P.H., Ronald N. Marcus, M.D., Robert D. McQuade, Ph.D., William H. Carson, Jr., M.D., Jean-Noel Beuzen, M.D.

Educational Objectives:

To demonstrate the differential risk of metabolic events among patients exposed to atypical antipsychotic agents

Summary:

Background: Recent evidence (1,2) suggests that certain atypical antipsychotics are associated with metabolic adverse events such as weight gain, and dyslipidemia. These adverse events may contribute to increased risk of cardiovascular disease. The STAR naturalistic trial provides the opportunity for a comparison of metabolic adverse events between aripiprazole and SOC treated patients

Methods: A total of 555 patients were equally randomized to open-label treatment of aripiprazole (10-30 mg/day) or Standard of Care (SOC) (olanzapine 5 - 20 mg/day, or quetiapine 100 - 800 mg/day or risperidone 2 - 8 mg/day) . Clinicians were free to select the Standard of Care agent most appropriate for the patient, a switch was however mandatory. Changes from baseline to Week 26 (LOCF) in levels of total HDL, LDL,cholesterol, triglycerides, glucose, and weight were analyzed using ANCOVA including treatment, fasting status and baseline value.

Results: At Week 26, a statistically significant larger mean decreases from baseline was observed in the aripiprazole group (20.3 mg/dL) versus the SOC group (7.7 mg/dL) ($p<0.001$). HDL-C rose by 2.0 mg/dl among aripipiprazole patients and 0.4 md/dl among SOC ($p=0.028$). Triglycerides decreased by 46.3 mg/dl and 13.0 mg/dl for aripiprazole and SOC respectively ($p<0.001$). LDL-C decreased by 13.3 mg/dl and 5.8 mg/dl for aripipiprazole and SOC respectively ($p<0.001$). Body weight decreased by 1.3 kg among aripiprazole patients and increased by 2.1 kg among SOC patients ($p<0.001$). Glucose changes were not significantly different (0.2 mg/dl for aripiprazole versus 3.3 mg/dl for SOC, $p= 0.146$).

Conclusion: Patients treated with aripiprazole experienced greater improvement versus SOC in the metabolic profile. This may correspond to clinically relevant reductions in subsequent diabetes and cardiovascular risk.

References:

1. 1 McQuade RD, Stock E, Marcus R, et al. A comparison of weight change during treatment with olanzapine or aripiprazole: results from a randomized, double-blind study. J Clin Psychiatry 2004;65 (Suppl 18) 48-56.

2. Meyer JM, Koro CE. The effects of antipsychotic therapy on serum lipids: a comprehensive review. Schizophr Res 2004;70:1-17.

NR392 Tuesday, May 23, 12:00 PM - 2:00 PM

Dyslipidemia Risk Differs According to Atypical Antipsychotic Use: A Review and Meta-Analysis

Gilbert L'Italien, Ph.D. *Bristol-Myers Squibb, 5 Research Parkway, Wallingford, CT, 06492*, John Newcomer, M.D., Vickie Tuomari, M.S., Hong J. Kan, Ph.D., Patricia Corey-Lisle, Ph.D., William Carson, M.D.

Educational Objectives:

Educational Objective: At the conclusion of this session, participants will gain an understanding of the relationship between the use of atypical antipsychotics and the risk for development of dyslipidemia among the major atypicals

Summary:

Background: The recent published literature (1) describing the relationship between dyslipidemias and the use of atypical antipsychotics provides us the opportunity to quantitatively summarize the available evidence using meta-analytic methods.

Methods: We conducted a comprehensive search of electronic databases (MEDLINE, Current Contents®) for studies published in the last 5 years with at least one atypical treatment for schizophrenia. Dyslipdemia was defined as an abnormal value of any fasting lipid measure (total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides) by ATP-III (2). Summary Odds Ratios(SOR) ±95% CI were computed from reported ORs for 6 atypicals (clozapine, olanzapine, risperidone, quetiapine, aripiprazole, ziprasidone) with 1 referent group: conventional antipsychotics. Mantel-Haenzel fixed-effects models were used to compute weighted SORs.

Results: A total of 5 primary studies comprising 53,480 patients were included. SORs for the association between dyslipidemia and clozapine use was 1.47(1.12-1.93). For olanzapine use, SOR = 1.41(1.14-1.74). For quetiapine use, SOR = 1.19(1.11-1.28). For risperidone use, SOR = 1.12(1.00-1.26). For ziprasidone use, SOR = 1.1(0.94-1.29); and for aripiprazole use, SOR = 0.82(0.67-1.00). Statistical tests of heterogeneity indicated that the SORs differed according to drug.

Conclusions: Results suggest differential risk for dyslipidemia among atypical agents favoring the newer drugs, aripiprazole and ziprasidone. Consideration of these differential risks should be included in therapeutic decisions for this patient population.

References:

1. Second generation (atypical antipsychotics and metabolic effects ' A comprehensive literature review. CNS Drugs 2005;19 Suppl 1:pp 1-93.
2. National Institutes of Health Third Report of the National Cholesterol Education Program Expert panel on detection, evaluation, and treatment of high blood cholesterol in adults. Adult Treatment Panel III. Bethesda MD, National Institutes of Health 2.

NR393 Tuesday, May 23, 12:00 PM - 2:00 PM

Olanzapine and Risperidone Treatment Response Prediction by Initial Assessment by the Five-Factor Structure of the Positive and Negative Syndrome Scale (PANSS)

Georges Brousse, M.D. *Clermont Ferrand*, Alexandre Meary, Anne-audrey Schmitt, Christophe Lancon, Marion Leboyer, Pierre-Michel Llorca, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to know that not only the subscores of PANSS but the factors of this scale at the begining of antipsychotics treatment are predictors of the response to this treatment

Summary:

Schizophrenia is a chronic disability that leads to significant residual morbidity. Treatment response studies would help to reduce therapeutics failures and long term prognosis of this severe and frequent disorder.

The aims of this study was to determine if the initial clinical assessment, particularly dimensional, by the five dimensions solutions (negative, positive, excitation, cognitive, and anxiety/depression factor) of the Positive and Negative Symptoms Scale (PANSS) can predict the short term drug response.

89 schizophrenic patients, according to DSMIV criteria, were prospectively assessed with the PANSS at day 0 and day 42 of an open label trial with olanzapine (52) and risperidone (37). A patient was considered as responder if he shows a diminution of 20% at the PANSS and a score less than 35 at the BPRS at day 42. The average of total, sub-scores, and five dimensions structure scores of the PANSS were compared between the two groups using a non parametric Man Whitney test and a regression analysis was realized between delta PANNS score and each dimensions score at J0.

28 patients were, as defined responders and 61 were non responders. The total (110,2 versus 95,4 P<0,01) and general (51,8 versus 44,6 p<0,5) score of the PANSS and the score of positive (30,0 versus 26.1) and excitation (20.5 versus 16.0) sub scores of the five dimensions factors were statistically different between non responders and responders at day 0 and were correlated to the response (r=0.93, r= 0.86, r=0.75, r=0.79). For responders there is a correlation between initials cognitive and negative scores and response (r=0.79, r=0.61). Curiously initial anxiety/depression factor doesn't differ between responders and non responder and is not correlated to the response.

Initial dimensional assessment, particularly anxiety/depression score, does not contribute to indicate predictive treatment response. General psychopathology and total PANSS score moderately elevated, predict treatment response.

References:

1. Lançon C, Reine G, Llorca PM, Auquier P. Validity and reliability of the French-language version of the Positive and Negative Syndrome Scale (PANSS). Act Psychiatr Scand 1999: 100:237-243.
2. Kay SR, Fiszbein A, Opler LA.

NR394 Tuesday, May 23, 12:00 PM - 2:00 PM

Clinical and Functional Improvements With Long-acting Risperidone: Interim Results in Patients With Schizophrenia

Julie C. Locklear, Pharm.D. *Ortho-McNeil Janssen Scientific Affairs, LLC, 1125 Trenton Harbourton Road, Titusville, NJ, 08560*, Lian Mao, Ph.D., Earle Bain, M.D., Stephen Rodriguez, M.S., Asli Memisoglu, Susan Vallow, M.A.

Educational Objectives:

1. Understand clinical characteristics of patients with schizophrenia initiated on long-acting risperidone
2. Understand the clinical and functional improvements for patients with schizophrenia initiated on long-acting risperidone from these interim results.

Summary:

Objective: To examine interim results for patients enrolled in an ongoing, 2-year observational study in patients with schizophrenia initiated on risperidone long-acting injection (RLAI; Risperidone® CONSTA®).

Methods: Adult patients with a diagnosis of schizophrenia who require treatment initiation of RLAI are eligible for enrollment.

Patient demographics, treatment history, reason for starting new treatment, Clinical Global Impressions of Severity (CGI-S), Global Assessment of Functioning (GAF), Personal and Social Performance (PSP), Strauss-Carpenter Levels of Functioning (LOF), quality of life (SF-36), and resource utilization are collected at baseline and prospectively every 3 months for 2 years.

Results: Interim, 6-month, data are available for 270 patients. The mean (± SD) age is 44.2±12.4 years, 65.2% are male, 71.9% have a diagnosis of paranoid schizophrenia, with a mean length of illness of 19.8±12.4 years. Most patients (73.0%) were initiated on a starting dose of RLAI 25 mg. The most common (51.9%) reason for initiating treatment with RLAI was insufficient response to previous therapy, followed by patient/family choice (44.1%), convenience (40.7%), and lack of compliance on previous therapy (40.4%). The average (±SD) duration between RLAI injections is 16.5±5.6 (median 14.2) days. Six-month (n=53) results showed clinical status (CGI-S) improved from 4.5±1.3 at baseline to 3.5±1.2 (P <0.001). Mean (±SD) PSP scores improved from 48.1±17.3 at baseline to 59.2±14.3 (P <0.0001). Mean (±SD) GAF scores improved from 48.7±15.2 at baseline to 56.6±12.9 (P<0.001). Functioning (LOF) and health-related quality-of-life (by SF-36) improvements at month 6 will also be presented. Percent of patients reporting at least 1 adverse event is 10.7%

Conclusions: Initial follow-up data from this ongoing observational study suggest that schizophrenia patients treated with RLAI are compliant and experience improvements in clinical and functional status. More data, including resource utilization, are being accrued to further explore these improvements.

Supported by Ortho-McNeil Janssen Scientific Affairs, LLC.

References:

1. Kennedy L, Craig A: Global registries for measuring pharmacoeconomic and quality-of-life outcomes. Pharmacoeconomics 2004; 22:551-568.

2. Franciosa JA: The potential role of community-based registries to complement the limited applicability of clinical trial results to the community setting: heart failure as an example. Am J Manag Care 2004; 10:487-492.

NR395 Tuesday, May 23, 12:00 PM - 2:00 PM

Remission in Schizophrenia: A Comparison of 2 Dose Regimens of Ziprasidone Versus Haloperidol Treatment in a 40-week Core and Three year Double-Blind Extension Study

Antony D. Loebel, M.D. *Pfizer Inc, 235 East 42nd Street, 235/10/14, New York, NM, 10017*, Lewis Warrington, M.D., Cynthia Siu, Ph.D., Jeffrey A. Lieberman, M.D.

Educational Objectives:

Participants will have a greater understanding of the long-term effectiveness of atypical antipsychotics compared with conventional agents, including differential effects on remission and quality of life.

Summary:

Objective: To compare the effectiveness of 2 dose regimens of ziprasidone with haloperidol in subjects with schizophrenia over a 40-week double-blind core and 3-year double-blind extension study.

Methods: Subjects completing the core study were eligible for a 3-year double-blind continuation study comparing 2 dose regimens of ziprasidone (BID 80-160 mg/d; N=72 or QD 80-120 mg/d; N=67) versus haloperidol (5-20 mg/d; N=47). The efficacy evaluation was based on schizophrenia remission criteria[1] which require maintenance, over 6 consecutive months, of ratings of mild or less (<=3) on 8 PANSS items. Remission and quality of life (QLS) over time were analyzed using Generalized Estimating Equation (GEE) methodology.

Results: Ziprasidone treatment was associated with higher rates of remission versus haloperidol (using severity criteria) at all visits during years 2-4. Compared to haloperidol, ziprasidone treatment resulted in a significantly higher proportion of patients meeting full remission criteria ($p<0.05$) in the final 6 months of the study. Both ziprasidone BID and QD groups showed significantly greater improvement in QLS scores than haloperidol over the 3-year extension phase. These differences were explained in part by improvement in remission status with ziprasidone ($p<0.001$ mediation coefficient).

Conclusions: In this randomized, double-blind, long-term (40-week core and 3-year extension) study, ziprasidone was associated with continued improvement in remission and quality of life, in contrast to haloperidol.

Support for this study was provided by Pfizer

References:

1. Lieberman JA et al. Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. N Eng J Med 2005;353:1209-23.

2. Andreasen NC, Carpenter WT, Kane JM et al. Remission in schizophrenia: Proposed criteria and rationale for consensus. Am J Psychiatry 2005;162:441-449.

NR396 Tuesday, May 23, 12:00 PM - 2:00 PM

Switch from atypical APs to long-acting risperidone: patient perspective

Emile-Roger Lombertie, Ph.D. *Centre hospitalier Esquirol, 15, rue du Dr. Raymond Marcland, LIMOGES CEDEX, 87025, France*, Annie Viala, Ph.D., Philippe Durst, Ph.D., Veronique Moreau-Mallet, Ph.D., Philippe Bouhours, Ph.D.

Educational Objectives:

This poster will enable the reader to understand the health-related improvements seen in patients with schizophrenia during treatment with a long-acting injectable atypical antipsychotic.

Summary:

Objective: To investigate the effects on patient satisfaction and health-related quality of life (QoL), of a direct transition from oral atypical antipsychotics to risperidone long-acting injectable (RLAI) in patients with schizophrenia or other psychotic disorders.

Methods: Adult patients who were clinically stable on their medication but required a change of treatment were given RLAI 25 mg (increased to 37.5 mg or 50 mg, if necessary) every 2 weeks for 6 months. Satisfaction with treatment was assessed at baseline and 6 months using a 5-point scale: very good, good, moderate, poor or very poor. QoL was assessed by the SF-36 questionnaire at baseline, 3 and 6 months.

Results: A subgroup analysis was performed with130 French patients (69% male, mean age 36±12 years). Patient satisfaction was improved after treatment with RLAI, and increases from baseline to endpoint occurred in the proportion of patients rating it as 'very good' (12% versus 30%). There were also significant increases from baseline to endpoint ($p<0.05$) in scores for almost all SF-36 domains.

Conclusion: The transition from oral atypical antipsychotics to RLAI was well accepted by patients in France. Patients showed significant improvements in their health-related quality of life and increased satisfaction with treatment.

References:

1. Moeller H, Llorca P, Sacchetti E, Martin S, Medori R, Parellada E. Efficacy and safety of direct transition to risperidone long-

acting injectable in patients treated with various antipsychotic therapies. Int Clin Psychopharmacol 2005;20(3):121-130.

2. Eerdekens M, Van Hove I, Remmerie B, Mannaert E. Pharmacokinetics and tolerability of long-acting risperidone in schizophrenia Schizophrenia Research 2004; 70: 91-100.

NR397 Tuesday, May 23, 12:00 PM - 2:00 PM

Assessing Depression and Nutritional Status of Community Dwelling Mexican American Elders and European American Elders

Ashley S. Love, D.P.H. *University of Texas at San Antonio, Health and Kinsiology, 6900 North 1604 West, San Antonio, TX, 78249*, Robert J. Love, D.O.

Educational Objectives:

Assessments are not routinely given to community dwelling elders to assess their global well-being. At the conclusion of this session, the participants will understand the importance of assessing depression and nutritional status of community dwelling elders. Participants will also appreciate that no significant depressive symptom differences were observed between MA and EA elders in this pilot study.

Summary:

Objective: To assess depression and nutritional status among elderly in the community-setting to determine if any differences are found between EA and MA elders to improve intervention programs.

Method: A cross-sectional design was used to sample 130 cognitively eligible community dwelling elders attending 9 nutrition centers in the Bexar County, TX. The interviews were completed by 116 elders using standard questionaires: Centers for Epidemiological Studies on Depression (CES-D) and other demographic/ health questions. Anthropometric measures such as height, weight, and body fat were measured.

Result: About 68% of the sample exhibited depressive symptom; however, there were no significant depressive symptom differences between MA and EA elders or between genders. Those who exhibited depressive symptoms ate less % of total fat (p= 0.041) and less % of saturated fat (p=.037) compared to those who did not show depressive symptoms. There was a trend for higher intakes of carbohydrates (p=.058) and lower intakes of fiber (p=.059) for those who were depressed.

Conclusions: Depressed elders in the community have different nutritional status than non-depressed elders regardless of race and gender. This study will provide a good stepping stone to create a comprehensive intervention program that can incorporate screening for depression and nutritional status.

References:

1. Amarantos, E, Martinez, A, Dwyer, J. Nutrition and quality of life in older adults. J of Gerontology 2001; 56A:54-64.

2. Chen, C. A Framework for Studying the Nutritional Health of Community-Dwelling Elders 2005; 54(1):13-21.

NR398 Tuesday, May 23, 12:00 PM - 2:00 PM

Treatment Persistence and Antipsychotic Therapy: Results of a Longitudinal Pharmacy Claims Database Analysis

Connie A. Lung, M.B.A. *Pfizer, Inc., 235 East 42nd Street, MS 6, New York, NY, 10017*, Antony D. Loebel, M.D., Ilise D. Lombardo, M.D., Brian Cuffel

Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand the challenge of medication adherence as a key issue in the effective treatment of patients diagnosed with schizophrenia.

Summary:

Objective: To compare treatment persistence among patients who were prescribed conventional and atypical antipsychotics.

Methods: Verispan claims data[1] (N=217,000 patients) were used to compare persistency (time on therapy with no interruption of greater than 1 month) in patients with schizophrenia having a new to market claim from October-December 2002, and then followed for 15 months. Univariate analyses were performed to evaluate the influence of demographic and clinical variables on treatment persistence.

Results: Among patients receiving a new prescription, regardless of diagnosis, mean duration of therapy fell into 3 groups: a low adherence group (mean duration 88 days: haloperidol), an intermediate adherence group (mean, 118-134 days: olanzapine, ziprasidone, risperidone, quetiapine), and a high adherence group (mean, 212 days: clozapine). Compared to haloperidol, the relative risk of discontinuation by 6 months was lower on clozapine (0.65), quetiapine (0.78), ziprasidone (0.83), risperidone (0.83), and olanzapine (0.85). Similar reductions in relative risk of premature discontinuation were observed for atypical antipsychotics versus haloperidol when the analysis was limited to patients diagnosed with schizophrenia. Antipsychotic persistency was not significantly influenced by age, gender, recency of diagnosis (new versus previous), whether patients were switching from a previous antipsychotic or were being treated for the first time.

Conclusions: Consistent with the results of the recent CATIE[2] trial, this claims database identified early discontinuation as a significant problem; but the current results differ in finding better adherence on atypical versus conventional antipsychotics.

References:

1. Verispan, Antipsychotic Persistency and Length of Therapy Study, July 2004.

2. Lieberman JA, et al: CATIE Investigators. Effectiveness of antipsychotic drugs in patients with chronic schizophrenia.N Engl J Med 2005;353:1209-1223.

NR399 Tuesday, May 23, 12:00 PM - 2:00 PM

Undertreatment of Dyslipidemia in Patients Treated With Atypical Antipsychotic Drugs Who are at High Risk for Coronary Heart Disease.

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Educational Objectives:

Despite increased attention placed on the identification and treatment of dyslipidemia as the primary target for reducing the incidence of coronary artery disease, the condition remains undiagnosed and untreated in in a significant number of patients seen by cardiologists and primary care physicians. The issue is important for psychiatric patients treated with atypical antipsychotics, because some of these drugs promote or worsen metabolic syndrome and thus increase the risk of coronary events. At the conclusion of the presentation, the participants should be able to recognize the magnitude and causes of undertreatment of dyslipidemia in high risk psychiatric patients.

Summary:

Objective: To determine whether psychiatric patients (pts) treated with atypical antipsychotics who are at high risk of coronary heart disease (CHD) receive appropriate primary target interventions for elevated low-density lipoprotein cholesterol (LDL-C) as defined by the National Cholesterol Eduction Panel (NCEP). Methods: 367 adults treated with atypical antipsychotic drugs randomly selected from consecutive psychiatric admissions to a single hospital underwent assessments evaluating the 10-year risk of CHD according to the NCEP scoring system The NCEP therapeutic target for LDL-C was calculated for pts with a CHD risk of 10% or greater. The records of pts with above-target LDL-C were reviewed to assess referrals for medical consultation, low- fat and low cholesterol diet, and pharmacologic interventions to lower the LDL-C. Results: 80 (22%) pts had a 10% or greater 10-year risk of CHD. The increased risk was associated with elevated triglyceride levels ($p<0.0001$) and current treatment with olanzapine ($p=0.019$) or quetiapine ($p=0.036$). 46 of the high-risk pts (57.5%) had LDL-C level above target. Patients with above-target LDL-C were younger ($p=0.009$) and more likely to smoke cigarettes ($p=0.037$). 28 of the high-risk pts with above-target LDL-C (61%) had no intervention to address dyslipidemia. The majority of patients receiving substandard care were diabetic or had a history of previous CHD events. Age, gender, ethnicity, psychiatric diagnoses, psychotropic drugs and features of the metabolic syndrome did not correlate with differences in care. Conclusions: These data suggest that dyslipidemia is frequently untreated in psychiatric pts who have the greatest vulnerability for CHD events. A knowledge deficit about risk assessment and LDL-C targets is the most likely explanation for this finding.

References:

1. Frolkis JP, Zyzanski SJ, Schwartz JM, et al. Physician noncomplinace with the 1993 national Cholesterol Education Program (NCEP-ATPII) Guidelines. Circulation 1998;98: 851-855.
2. Henderson DC, Nquyen DD, Copeland PM, et al. Clozapine, diabetes mellitus, hyperlipidemia, and cardiovascular risks and mortality. J Clin Psychiatry 2005;66:1116-1121.

NR400 Tuesday, May 23, 12:00 PM - 2:00 PM

A Six-week, U.S.-Based Placebo-Controlled Study on the Efficacy and Tolerability of Two Fixed Dosages of Oral Paliperidone Extended-Release Tablets in the Treatment of Acute Schizophrenia

Stephen R. Marder, M.D. *Semel Insititue at UCLA and the VA VISN 22 Mental Illness Research, Education, and Clinical Center, M1 RECC 210A 11301 Wilshire Boulevard, Los Angeles, CA, 90073-1003*, Michelle Kramer, M.D., Lisa Ford, M.D., Els Eerdekens, M.S.C., Pilar Lim, Ph.D., Marielle Eerdekens, M.D.

Educational Objectives:

At the conclusion of this presentation, participants should be able to describe the efficacy and tolerability of the investigational drug paliperidone extended-release, and the effect on functioning during the treatment of acute schizophrenia as assessed using the Personal and Social Performance Scale.

Summary:

Objective: This study in patients with acute schizophrenia examined the efficacy, safety and effect on patient functioning of investigational paliperidone extended-release (paliperidone Extended Release) tablets.

Method: This double-blind, parallel group, placebo- and active-controlled, dose-response study randomized patients (n=444; age ≥18 years) to receive paliperidone Extended Release 6mg or 12mg, placebo or olanzapine 10mg daily. Olanzapine was included for assay sensitivity only and the study powered to assess efficacy of paliperidone Extended Release versus placebo.

Results: The intention-to-treat (ITT) set (n=432) was 55% black with mean age=41.6y±10.7. Mean PANSS total score (93.7±11.9 at baseline in ITT group) improved at endpoint for paliperidone Extended Release versus placebo (6mg=-15.7±18.9 [p=0.006], 12mg=-17.5±19.8 [p<0.001], placebo=-8.0±21.5 [olanzapine change=-18.4±19.9]). Personal and Social Performance Scale scores improved at endpoint for both paliperidone Extended Release groups versus placebo (6mg=8.8±13.9 [p=0.008], 12mg= 6.6±13.1 [p=0.214], placebo=2.9±13.0). Treatment-emergent adverse events (TEAEs) occurring >3% more than with placebo were headache and dry mouth (paliperidone Extended Release), and somnolence, anorexia and increased serum glutamic oxaloacetic transaminase (olanzapine). TEAE-EPS were comparable in the paliperidone Extended Release 6mg, olanzapine and placebo groups, but higher with paliperidone Extended Release 12mg. Serious AE frequency was 8% with paliperidone Extended Release, 11% with olanzapine and 10% with placebo.

Conclusions: In this study, paliperidone Extended Release 6mg and 12mg was effective and generally well tolerated.

References:

1. Falkai P, Wobrock T, Lieberman J, et al.: World Federation of Societies of Biological Psychiatry (WFSBP) guidelines for biological treatment of schizophrenia, Part 1: acute treatment of schizophrenia. World J Biol Psychiatry 2005; 6(3):132-191.
2. Practice guidelines for the treatment of patients with schizophrenia (2nd Edition), February 2004. Available at: http://www.psych.org/psych_pract/treatg/pg/Practice20Guidelines8904/Schizophrenia_2e.pdf.

NR401 Tuesday, May 23, 12:00 PM - 2:00 PM

The Effectiveness of Aripiprazole in Schizophrenia Patients With High or Low Agitation

Stephen R. Marder, M.D. *VA Greater LA Health Care System, M1 RECC 210A 11301 Wilshire Boulevard, Los Angeles, CA, 90073-1003*, David Crandall, Ph.D., Joseph Pultz, William H. Carson, Jr., M.D., Rolando Gutierrez-Esteinou, Quynh Van Tran, Ronald N. Marcus, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to appreciate that acute episodes of schizophrenia are comprised of a spectrum of symptoms, including various levels of agitation. They should be aware that aripiprazole significantly reduces the symptoms of psychosis and agitation in patients with either high or low agitation (with or without concomitant benzodiazepine use), as demonstrated by a pooled analysis of efficacy data from the first 4 weeks of 4 placebo-controlled trials for schizophrenia.

Summary:

Objective: Determine if baseline symptoms of agitation impact the overall effectiveness of aripiprazole in patients with acute schizophrenia.

Methods: Pooled analyses were performed on efficacy data from the first 4 weeks of 4 randomized, double-blind trials in patients with acute schizophrenia receiving aripiprazole 10-30 mg/d (n = 785) or placebo (n = 296). Patients were divided into groups experiencing high or low levels of agitation at baseline. High agitation was defined as a PANSS Excited Component (PEC) score ≥14 and a score of ≥4 on at least 1 PEC item. Change from baseline through Week 4 in PANSS total, PEC, and Clinical Global Impression-Improvement (CGI-I) scores were measured. Mean change from baseline comparisons were analyzed using an AN-

COVA model controlling for treatment, protocol, and baseline value.

Results: Regardless of agitation level at baseline, aripiprazole significantly improved PANSS total, PEC, and CGI-I scores at endpoint, compared with placebo ($P < 0.05$). Differences between aripiprazole and placebo remained significant for all 3 outcomes measures following stratification of baseline agitation scores. The proportion of patients using benzodiazepines was not significantly different between aripiprazole and placebo groups.

Conclusions: Aripiprazole was associated with overall symptomatic improvement in patients with acute schizophrenia, regardless of baseline agitation status. In addition, aripiprazole was not associated with increased benzodiazepine use, as compared with placebo.

References:

1. Kane JM, Carson WH, Saha AR, et al: Efficacy and safety of aripiprazole and haloperidol versus placebo in patients with schizophrenia and schizoaffective disorder. J Clin Psychiatry 2002; 63:763-771.
2. Potkin SG, Saha AR, Kujawa MJ, et al: Aripiprazole, an antipsychotic with a novel mechanism of action, and risperidone vs placebo in patients with schizophrenia and schizoaffective disorder. Arch Gen Psychiatry 2003; 60:681-690.

NR402 Tuesday, May 23, 12:00 PM - 2:00 PM

Antipsychotic Medication Gaps in Dual Diagnosis

Jeffrey Markowitz, Ph.D. *Health Data Analytics, 35 Arnold Drive, Princeton Jct., NJ, 08550*, Julie Locklear, Pharm.D.. Luella Engelhart, M.A.

Educational Objectives:

1. Understand patients with schizophrenia and dual diagnosis experience gaps in antipsychotic medication use.
2. Understand the importance of identifying patients with dual diagnosis who are likely to experience longer periods of antipsychotic medication gaps.

Summary:

Introduction: The lifetime prevalence of dual diagnosis in schizophrenia ranges from 10% to 60%. A dual diagnosis of schizophrenia plus alcohol/substance abuse/dependence has been linked to poor patient outcomes and higher health care costs. This study compared compliance, based on medication gaps in antipsychotic medication (AP) use, in patients with schizophrenia with and without dual diagnosis.

Methods: We used a 20% random sample of California Medicaid (Medi-Cal) claims data from between 1996 and 2002 to identify patients with schizophrenia with and without dual diagnosis, using both primary and secondary ICD-9 codes (DUAL and SCH, respectively). Antipsychotic medication gaps were derived from prescription date and days' supply. We studied number of AP treatment gaps and mean, maximum, and sum of all gap days. Unadjusted and demographic-adjusted mean gap scores were compared between DUAL and SCH over a 1-year study period.

Results: 3133 subjects were studied: mean (±SD) age, 41.7 ± 10.8 years; 60.4% male; 704 (22.5%) DUAL; and 2429 (77.5%) SCH. Mean number of gaps was approximately 4 for each group. Mean (±SD) gap duration was higher for DUAL (27.6±53.4) versus SCH (24.1±52.7), although not significant. Unadjusted maximum gap days (±SD) were significantly higher in DUAL (50.3±69.8) versus SCH (41.4±67.2), $P = 0.0022$. Unadjusted summed gap days (±SD) was also significantly higher in DUAL (82.0±88.1) versus SCH (66.7±80.7), $P < 0.0001$. Multivariate analyses controlling for demographics confirmed these results.

Discussion: These results likely represent an underestimate of the true prevalence of schizophrenia plus alcohol/substance abuse in this patient population. Both groups experienced gaps in AP. Patients with dual diagnosis appear to have more days of noncompliance per year versus patients with schizophrenia. This is likely to be associated with poorer patient outcomes and more costly health care.

Supported by Ortho-McNeil Janssen Scientific Affairs, LLC.

References:

1. Weiden PJ, Kozma C, Grogg A, Locklear J: Partial compliance and risk of rehospitalization among California Medicaid patients with schizophrenia. Psychiatr Serv 2004; 55: 886-891.
2. Green AL: Schizophrenia and comorbid substance use disorder: effects of antipsychotics. J Clin Psychiatry 2005; 66(Suppl 6):21-26.

NR403 Tuesday, May 23, 12:00 PM - 2:00 PM

Stability and Validity of Two Memory-Based Subtypes of Schizophrenia

Stephanie McDermid Vaz, Ph.D. *York University, Psychology, 25 Trailwood Drive, Suite 801, Mississauga, ON, L4Z 3K9, Canada*, R. Walter Heinrichs, Ph.D.

Educational Objectives:

At the conclusion of the session, the participant should have an understanding of verbal memory subtyping in schizophrenia, as well as the importance of demonstrating cognitive validity and stability in candidate typologies.

Summary:

Objective: To assess memory-based subtyping as an organizing principle for reducing the heterogeneity of schizophrenia.

Method: The temporal stability and cognitive validity of: (a) a cortical-subcortical-normative typology (Turetsky et al., 2002) derived from dementia patients' scores on the California Verbal Learning Test (CVLT) and (b) a memory impairment-based dichotomy based on a CVLT summary score (McDermid Vaz & Heinrichs, 2002) were evaluated. These memory subtypes were examined in 102 atypical neuroleptic naUïve schizophrenia patients receiving conventional anti-psychotic medication, with 55 patients assessed a second time 3 years later.

Results: The cortical-subcortical-normative typology (Turetsky et al., 2002) was partially replicated in this sample of schizophrenia patients. However, the typology demonstrated poor cognitive validity and modest stability at 3-year follow-up. Analysis of the McDermid Vaz and Heinrichs (2002) dichotomy, which identified patients as either memory-impaired or memory-unimpaired showed adequate cognitive validity; however stability was also modest over time.

Conclusions: Collectively, the results provide preliminary support that memory-based subtyping might be effective in organizing schizophrenia into more homogeneous groups for clinical and etiological research. Both methods yield potentially valuable illness distinctions, but require modification and refinement, especially in terms of discriminating patients with persisting and more transitory forms of memory impairment.

References:

1. McDermid Vaz, SA & Heinrichs, RW: Schizophrenia and memory impairment: Evidence for a neurocognitive subtype. Psychiatry Research 2002; 113: 93-105.
2. Turetsky BI et al.: Memory-delineated subtypes of schizophrenia: Relationship to clinical, neuroanatomical, and neurophysiological measures. Neuropsychology 2002; 16: 481-490.

NR404 Tuesday, May 23, 12:00 PM - 2:00 PM

Functional Recovery in Patients With First-Episode Psychosis Treated With Long-Acting Risperidone as a First-Line Treatment: Six-month Interim Analyses

Rossella Medori *Janssen Pharmaceutica, Turnhoutseweg 30, Beerse, 2340, Belgium*, Piet Oosthuizen, Liezl Koen, Dana Niehaus, Robin Emsley

Educational Objectives:

At the end of this presentation the reader should be able to describe the effect of treatment with long-acting risperidone on functioning in patients with first-episode psychosis.

Summary:

Objectives: Assess changes in patient function in first-episode psychosis patients treated with long-acting risperidone (LAR); pre-specified 6-month interim analyses of a 24-month, open-label study.

Methods: LAR 25-50mg was administered every 2 weeks following 1 week of risperidone oro-dispersible (1-3mg). Assessments included change from baseline to 6 months on CGI-S, Social and Occupational Functional Assessment (SOFAS), Social Functioning-12 (SF-12; Mental Component Summary [MCS], Physical Component Summary [PCS]) and Patient Global Impression-Severity (PGI-S) scales and Calgary Depression Scale Schizophrenia (CDSS).

Results: Forty-three (86%) subjects (mean age=25.3±7.3 years) completed 6 months treatment. Reasons for discontinuation included consent withdrawal (n=1), injection refusal (n=1), felt no need to continue (n=2), insufficient response (n=1), lost to follow-up (n=1) and other (n=1). Improvement in CGI-S was observed at endpoint (-2.6±1.4 [p<0.001]). Statistically and clinically significant functional improvements were observed on the SOFAS (24.8±14.9 [p<0.001]) and MCS (11.3±14.2 [p<0.001]). The PCS score slightly declined (-6.1±10.5 [p=0.0017]). CDSS score improved slightly (-0.6±4.2 [p=0.053]) and concomitant medication use (e.g. antidepressants, anticholinergic agents) was low. PGI-S score improved from baseline to endpoint (-1.1 ± 1.4 [p<0.001]).

Conclusions: These interim data suggest that functional improvements accompany the clinical improvement[1] observed in first-episode patients treated with LAR.

References

1. Emsley R, Oosthuizen P, Koen L, Niehaus D, Medori R. Safety and efficacy of long-acting risperidone as a first-line treatment for first-episode schizophrenia: 6-month interim analyses. Poster presented at Winter Workshop on Schizophrenia, Davos, Switzerland, 2006.

References:

1. Emsley R, Oosthuizen P: Evidence-based pharmacotherapy of schizophrenia. Int J Neuropsychopharmacol. 2004; 7(2):219-238.

2. Practice guidelines for the treatment of patients with schizophrenia (2nd Edition), February 2004. Available at: http://www.psych.org/psych_pract/treatg/pg/Practice20Guidelines8904/Schizophrenia_2e.pdf.

NR405 Tuesday, May 23, 12:00 PM - 2:00 PM

Long-Term Effects of Aripiprazole on the Lipid Profiles of Patients With Schizophrenia in a 26-Week Placebo-Controlled Trial

Jonathan M. Meyer, M.D. *VA SDH S, 3350 La Jolla Village Dr. (116-A), San Diego, CA, 92161*, Aneta Fornal, Pharm.D., Stephen Kaplita, M.S., Andy Forbes, Ph.D., Frederick Grossman, D.O., Andrei Pikalov, M.D., Ronald Marcus, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to list the detrimental changes in lipid levels that can occur with the use of certain antipsychotic medications for schizophrenia. They should also be able to appreciate that treatment of schizophrenia with aripiprazole is not associated with abnormal lipid levels, as demonstrated by analysis of a placebo-controlled 26-week trial for schizophrenia.

Summary:

Objective: Assess serum lipid level changes in patients with stabilized chronic schizophrenia treated with aripiprazole in a 26-week, randomized, double-blind, placebo-controlled trial. The FDA requested these analyses.

Methods: Incidences of treatment-emergent abnormal lipid levels associated with aripiprazole 15mg/d (n=153) or placebo (n=153) were assessed at Weeks 6, 18, and 26. Statistical differences were compared using the Fisher's Exact Test. The FDA requested that thresholds for abnormal lipid values (total cholesterol [TC] ≥240mg/dL, low-density lipoprotein [LDL] ≥160mg/dL, high-density lipoprotein [HDL] <40mg/dL, or triglycerides ≥200mg/dL) be based on guidelines from the NCEP ATP III. Mean changes (baseline-to-endpoint) in lipid levels were analyzed by ANCOVA.

Results: Total pooled incidences of abnormal fasting and nonfasting lipid levels did not differ significantly between aripiprazole- and placebo-treated patients: TC = 20/142 (14.1%) aripiprazole, 10/138 (7.2%) placebo; LDL = 12/139 (8.6%) aripiprazole, 10/137 (7.3%) placebo; HDL = 47/142 (33.1%) aripiprazole, 53/138 (38.4%) placebo; triglycerides = 33/142 (23.2%) aripiprazole, 32/138 (23.2%) placebo. Mean changes (baseline-to-endpoint) in lipid levels were also not significantly different between aripiprazole- and placebo-treated patients: TC (mean [SE]) = -11.8mg/dL (2.9) aripiprazole, -1.4mg/dL (2.5) placebo; LDL = -7.5mg/dL (2.6) aripiprazole, -2.0mg/dL (2.2) placebo; HDL = -0.4mg/dL (1.2) aripiprazole, -0.0mg/dL (0.9) placebo; triglycerides = -24.1mg/dL (10.3) aripiprazole, 2.2mg/dL (6.5) placebo. When patients were divided into fasting and nonfasting groups, incidences of abnormal lipid levels remained nonsignificant between aripiprazole and placebo. Significantly reduced TC and LDL levels were observed in nonfasting patients on aripiprazole, compared with placebo ($P<0.05$). No other significant differences in lipid levels were observed between aripiprazole and placebo for fasting or nonfasting groups.

Conclusion: Patients with schizophrenia who received long-term treatment with aripiprazole had similar lipid profiles to those receiving placebo.

References:

1. Marder SR, McQuade RD, Stock E, et al: Aripiprazole in the treatment of schizophrenia: safety and tolerability in short-term, placebo-controlled trials. Schizophr Res 2003; 61:123-136.

2. National Institutes of Health: Third Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Adult Treatment Panel III. Bethesda, MD, National Institutes of Health.

NR406 Tuesday, May 23, 12:00 PM - 2:00 PM

Barriers to Recruitment Among Middle- Aged and Older Persons With Schizophrenia in a Medication Adherence Intervention Study

Dinesh Mittal, M.D. *Veterans Affairs Medical Center, 2200 Fort Roots Drive, Little Rock, AR, 72114*, Jonathan Lacro, Pharm.D., Maureen Henry, M.S., Francis Hamilton, M.P.H., Richard R. Owen, Jr., M.D.

Educational Objectives:

The primary objective of the study is to describe barriers to recruitment in medication adherence intervention studies among middle- aged and older persons with schizophrenia. We also describe the rates of non-adherence among recently hospitalized middle- aged and older persons with schizophrenia.

Summary:

Objective: The primary objective of the study is to describe barriers to recruitment in medication adherence intervention studies among middle- aged and older persons with schizophrenia. We also describe the rates of non-adherence among recently hospitalized middle- aged and older persons with schizophrenia.

Methods: Potential participants were approached in the acute psychiatric units at the Central Arkansas Veterans Healthcare System for a non-pharmacological medication adherence study. The inpatient staff referred the potential participants. Participants were recruited based on the following inclusion & exclusion criteria: (1) age over 40 years with a DSM-IV diagnosis of Schizophrenia or Schizoaffective disorder and current prescription for maintenance therapy with antipsychotic medication, (2) have means to return to the outpatient clinic and access to a telephone at the residing facility, (3) not have a clinical diagnosis of dementia, (4) have the capacity to understand the nature of the study and sign an informed consent document. Once this information was obtained, eligible participants were given the opportunity to participate.

Results: Out of the 130 potential participants approached, 49 participants were eligible to participate. However, only 26 consented, 16 refused and seven had other reasons. The top three reasons for ineligibility included inability to return to clinic or not having access to the telephone (39), lacking capacity to consent (19) and refusal (17). The participants reported not taking their medications on an average 3.15 days out of the last week and took medications as prescribed only 21-40% times.

Conclusions: High rates of logistical barriers (transportation and access to telephone), capacity to consent and refusal limited participation of veterans in this medication adherence study. Among those who consented, high rates of non-adherence were observed among middle-aged and older persons with schizophrenia.

References:

1. Loughland CM, Carr VJ, Lewin TJ, Barnard RE, Chapman JL, Walton JM:Potential sampling and recruitment source impacts in schizophrenia research.Psychiatry Res. 2004 Feb 15;125(2):117-27.
2. Keith SJ.Evaluating characteristics of patient selection and dropout rates.J Clin Psychiatry. 2001;62 Suppl 9:11-4; discussion 15-6.

NR407 Tuesday, May 23, 12:00 PM - 2:00 PM

Police Actions as Forms of Social Support to Persons with a Mental Illness

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Educational Objectives:

At the conclusion of the presentation, the participant should: have a greater understanding of the work done by police officers in support of persons with a mental illness; be able to identify five forms of social support; be able to describe the constant comparative method of data analysis; and have learned about the contribution that qualitative research can make to furthering knowledge regarding issues of importance to psychiatry.

Summary:

Police contact is often the means by which persons with a mental illness (PwMI) access treatment and support services. Advocacy efforts have resulted in strengthening community supports for PwMI including the proliferation of police/mental health liaison initiatives such as crisis intervention teams. *Objective*: To aid in identifying the mechanisms by which such programs are helpful, this study sought to delineate the ways in which officers' actions constitute forms of social support. *Method*: Interviews were conducted with a convenience sample of 15 police officers of varied ranks from two Ontario police agencies. Drawing on Cutrona and Russell's (1990) framework that posits five types of supportive behaviours (emotional, social integration or network, esteem, tangible aid, and informational), data were analyzed using a grounded theory approach involving the constant comparative method of analysis (see Strauss & Corbin, 1998). *Results*: Police officers provide all five forms of social support. *Conclusion*: Regardless of whether or not they are involved in formalized police/mental health liaison efforts, police officers have a pivotal role in supporting PwMI.

References:

1. Cutrona CE, Russell, DW: Type of Social Support and Specific Stress: Toward a Theory of Optimal Matching. In Social Support: An Interactional View, edited by Sarason BR, Sarason IG, Pierce GR, New York, Wiley, 1990, pp319-366.
2. Strauss AL, Corbin J: Basics of Qualitative Research. Thousand Oaks, CA, Sage, 1988.

NR408 Tuesday, May 23, 12:00 PM - 2:00 PM

Genetic association analysis between the BDNF gene polymorphism (Val66Met) and schizophrenia

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to demonstrate clinical implications.

Summary:

Rationale: Brain-derived neurotrophic factor (BDNF) plays an important role in the development and maintenance of adult neurons and are important regulators of synaptic plasticity in human brain. It is also reported that the transneuronal transfer of BDNF is dependent on neuronal activity, suggesting that BDNF plays an important role in neurotransmission (Science 291, 2419-2423, 2001). The BDNF Val66Met polymorphism affects human memory and hippocampal function (Cell 112, 257-269, 2003). Recently, a positive association between the BDNF Val66Met polymorphism and schizophrenia in Scottish population was reported (Mol Psychiatry 10, 208-212, 2005). In the present study, we tried to replicate that finding in a Japanese case-control sample. *Material and Methods*: Our sample includes 211 patients with schizophrenia (DSM-IV) and 205 normal controls. Informed consent was a premise for participation, and this study was approved by the Ethics Committee of the University of Occupational and Environmental Health. Genomic DNA was extracted from 10-ml aliquots of EDTA-anticoagulated venous blood following the standard procedures. Genotyping was assessed by the TaqMan allele-specific assay method using ABI PRISM® 7000 (Applied Biosystems). Differences in allele and genotype distribution between cases and controls were evaluated using the χ^2 test. *Results*: No significant association between the BDNF Val66Met polymorphism and schizophrenia was found (genotype: $\chi^2 = 2.33$, df = 2, $p = 0.31$; allele: $\chi^2 = 1.34$, df = 1, $p = 0.25$). *Conclusion*: Our results suggest

that it is unlikely that the BDNF Val66Met polymorphism is associated with schizophrenia in our sample.

References:

1. Science 291, 2419-2423, 2001.
2. Mol Psychiatry 10, 208-212, 2005.

NR409 Tuesday, May 23, 12:00 PM - 2:00 PM

Low Rates of Treatment for Metabolic Disorders in the CATIE Schizophrenia Trial at Baseline: Healthcare Disparities in Schizophrenia

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the low treatment prevalence among individuals with schizophrenia who suffer from diabetes, hypertension or hyperlipidemia.

Summary:

Background:

The most recent data from the large (N=1460, mean age 40.6 years) NIMH-sponsored CATIE schizophrenia trial indicate that the metabolic syndrome (NCEP updated definition) is present in 42.7% of the CATIE sample at baseline (McEvoy et al, 2005), which is nearly *twice* the prevalence rate in the general population ages 40-49 years. We examined the proportion of the CATIE schizophrenia subjects who met criteria for one of the major metabolic disorders (diabetes, hyperlipidemia, and hypertension) and were or were *not* receiving treatment at the time of enrollment into the study.

Methods:

We analyzed the baseline data from the 57-site CATIE schizophrenia trial for the number of patients meeting clinical and laboratory diagnostic criteria for diabetes, hyperlipidemia, and hypertension, and calculated the percentage of those subjects at enrollment who were receiving a hypoglycemic agent, a statin, or an antihypertensive agent, respectively. We also examined the relationship of sex, race, and ethnicity to the rates of treatment for those disorders.

Results:

a) Diabetes: Of the 85 subjects with diabetes, 45.3% of the diabetic schizophrenia patients were *not* receiving treatment.

b) Hyperlipidemia: Of the 471 patients with elevated fasting lipid levels, 89.4% were *not* receiving a statin.

c) Hypertension: Of 550 patients who met criteria for hypertension, 62.4% were *not* receiving any antihypertensive. Gender and racial/ethnic breakdowns will be presented at the meeting.

Conclusion:

A high proportion of the CATIE Trial schizophrenia sample was *not* receiving appropriate and standard treatment for their metabolic disorder at the time of enrollment. These data are suggestive of health disparities reflected in the low rates of access to standard medical treatments, despite the high prevalence of the metabolic disorders observed in this schizophrenia sample.

References:

1. Book - Meyer JM, Nasrallah HA (Eds): Medical Illness and Schizophrenia. American Psychiatric Press, 2003.
2. Journal Article - McEvoy J, et al. Prevalence of the Metabolic Syndrome in Patients with Schizophrenia. Baseline results from the CATIE. Schizophrenia Research 2005; 80:9-32.

NR410 Tuesday, May 23, 12:00 PM - 2:00 PM

Improvement of Non-HDL Cholesterol Levels Among Patients Randomized to Aripiprazole Versus Olanzapine

John W. Newcomer, M.D. *Washington University School of Medicine, 660 South Euclid Avenue, Box 8134, St. Louis, MO, 63110-1002*, Gilbert L'Italien, Ph.D., Estelle D. Vester-Blokland, M.D., Robert D. McQuade, Ph.D., William H. Carson, Jr., Ph.D., Ronald N. Marcus, M.D.

Educational Objectives:

To describe the impact of certain atypical antipsychotics on the levels of important cardiovascular risk factors

Summary:

Background: Non-HDL cholesterol (non-HDL-c) is a significant and independent predictor of cardiovascular events (1-3), with a 10-mg/dL increase in non-HDL-c corresponding to 34% increased risk for myocardial infarction (3). This study compares changes in non-HDL-c among schizophrenia patients with abnormal values randomized to either aripiprazole or olanzapine.

Methods: Mean change from baseline in non-HDL-c was compared between treatments at 26 weeks (LOCF) by ANOVA in a post-hoc pooled analysis using aripiprazole clinical trial data for patients with baseline abnormal fasting values of non-HDL-c >130 mg/dL and a Body Mass Index (BMI) exceeding 25 kg/m^2.

Results: The mean (± SE) change from baseline in non-HDL-C was statistically significant ($P < 0.001$) with an increase of 6.4 (± 2.4) mg/dL for olanzapine (n = 155) and decrease of 12.7 (± 2.6) mg/dL for aripiprazole (n = 135). In higher-risk patients with BMI >27 kg/m^2 and non-HDL-c >160 mg/dL, mean change from baseline was -0.27 (± 3.9) and -17.4 (± 4.1) mg/dL for olanzapine and aripiprazole, respectively ($P = 0.003$). Net change between treatments in mean non-HDL-c was 19.1 mg/dL and 17.1 mg/dL for both main and high-risk subset groups respectively, favoring aripiprazole.

Conclusions: Patients randomized to aripiprazole treatment demonstrated clinically significant improvement in levels in non-HDL-c, in comparison to baseline. Olanzapine was associated with no clinical improvement from baseline non-HDL-c, highlighting the need for consideration of cardiovascular risk when prescribing atypical antipsychotic medications.

References:

1. Schulze et al: Joint role of non-HDL cholesterol and glycated haemoglobin in predicting future coronary heart disease events among women with type II diabetes Diabetologia 2004; 47:2129-2136.
2. Jiang et al: Non-HDL cholesterol and apolipoprotein b predict cardiovascular disease events among men with type II diabetes. Diabetes Care 2004; 27:1991-1997.

NR411 Tuesday, May 23, 12:00 PM - 2:00 PM

Effectiveness of Antipsychotic Treatment in Outpatients With Schizophrenia: 36- Month Results from the Schizophrenia Outpatients Health Outcomes (SOHO) Study

Diego Novick, M.D. *Eli Lilly and Company Limited, Erl Wood Manor, Sunninghill Road, Windlesham, GU20 6PH, United Kingdom*, Josep M. Haro, M.D., Jacqueline Brown, M.D., David Suarez, M.D., Mark Ratcliffe, M.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to understand the relative effectiveness of antipsychotic medications in the outpatient setting.

Summary:

Objectives: To compare the relative effectiveness, in terms of treatment discontinuation, of olanzapine, resperidone, quetiapine, amilsupride, clozapine, oral and depot typical antipsychotic medications in outpatients with schizophrenia during 3 years follow-up.

Methods: SOHO[1] is a 3-year, prospective, observational study of antipsychotic treatment. Treatment discontinuation was defined as discontinuing, adding to or switching the medication prescribed at baseline. A Kaplan Meier estimation of the time to medication discontinuation was plotted.

Results: 10, 972 patients were enrolled and 7728 patients who initiated antipsychotic monotherapy at baseline were included in this analysis. Approximately 42% of the patients discontinued the medication initiated at baseline before three years: quetiapine (66%), typical antipsychotics (53%), depot typical (50%) amisulpride (50%), risperidone (42%) olanzapine (36%) and clozapine (33%).[2]

A Cox regression showed that patients taking quetiapine (Hazard ratio 2.21; 95% CI: 1.95-2.5), amisulpride (1.62; 1.33-1.99), oral typicals (1.69; 1.46-1.96), depot typicals (1.42; 1.19-1.70) and risperidone (1.28; 1.16-1.42), had an increased risk of discontinuing their baseline medication compared to patients taking olanzapine. There were no statistically significant differences between the olanzapine and clozapine groups (0.82; 0.65-1.02).

Conclusions: Treatment effectiveness varied among medications. Clozapine and olanzapine were the most effective in terms of the rates of discontinuation.

References:

1. Haro JM, Edgell ET, Jones PB, Alonso J, Gavart S, Gregor KJ, Wright P, Knapp M, on behalf of the SOHO Study Group. SOHO Study: rationale, methods and recruitment. Acta Psychiatrica Scandinavica 2003;107(3):222-32.
2. Lieberman JA, Stroup TS, McEvoy JP, Swartz MS, Rosenbeck RA, Keefe RSE, Davis SM, Davis CE, Lebowitz BD, Severe J, Hsiao JK, for the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) Investigators. Effectiveness of Antipsychotic Dr.

NR412 Tuesday, May 23, 12:00 PM - 2:00 PM

Factors Associated with Risk of Relapse in Schizophrenia: 36 Month Results from the Schizophrenia Outpatients Health Outcomes (SOHO) Study

Diego Novick, M.D. *Eli Lilly and Company Limited, Erl Wood Manor, Sunninghill Road, Windlesham, GU20 6PH, United Kingdom*, Josep M. Haro, M.D., David Suarez, M.D., Mark C. Ratcliffe, M.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to understand the factors associated with relapse in the outpatient setting.

Summary:

Objectives: To analyse the frequency and baseline factors associated with risk of relapse during three years follow-up.

Methods: SOHO[1,2] is a 3-year, prospective, observational study of antipsychotic treatment outcomes.

Relapse was defined as i) an increase in the CGI score of 2 points, when the minimum score in any evaluation was 3 or less, ii) an increase in the CGI score of 1 points when the minimum score was 4 or more, or iii) admission to an inpatient service. The increment in CGI score had to lead to the patient being at least moderately ill (CGI ≥4).

Results: 10,972 patients were enrolled and 9,569 patients were included in the analysis; 2231 patients (23%) relapsed. Paid employment (RR: 0.799; 95% CI: 0.707-0.903), was associated to lower risk of relapse. Higher CGI severity at baseline (1.160; 1.103-1.221) was associated to higher risk. Taking Quetiapine (1.656; 1.417-1.936), Risperidone (1.171; 1.042-1.316), Oral Typicals (1.304; 1.096-1.551), Depot Typicals (1.637; 1.360-1.971) and Amilsupride (1.368; 1.080-1.732) was associated with a higher risk of relapse compared to patients taking Olanzapine. There were no differences between Olanzapine and Clozapine.

Conclusions: 23% of patients relapsed. Employment status and clinical severity were associated with relapse. Clozapine and Olanzapine were associated to lower risk of relapse.

References:

1. Haro JM, Edgell ET, Jones PB, Alonso J, Gavart S, Gregor KJ, Wright P, Knapp M, on behalf of the SOHO Study Group. SOHO Study: rationale, methods and recruitment. Acta Psychiatrica Scandinavica 2003;107(3):222-32.
2. Haro JM, Edgell ET, Frewer P, Alonso J, Jones PB on behalf of the SOHO Study Group. The European Schizophrenia Outpatient Health Outcomes Study: baseline findings across country and treatment. Acta Psychiatr Scand 2003; 107 (Suppl 416):1-9.

NR413 Tuesday, May 23, 12:00 PM - 2:00 PM

Factors Associated with Remission in Schizophrenia: 36-Month Results From the Schizophrenia Outpatients Health Outcomes (SOHO) Study

Diego Novick, M.D. *Eli Lilly and Company Limited, Erl Wood Manor, Sunninghill Road, Windlesham, GU20 6PH, United Kingdom*, Josep M. Haro, M.D., Cees J. Slooff, M.D., David Suarez, M.D., Liam Kennedy, M.S., Maarten Boomsma, M.D., Jacqueline Brown, M.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to understand the factors associated with achieving remission in the outpatient setting.

Summary:

Objectives: To analyse the frequency and factors associated with achieving remission during 3 years follow-up.

Methods: (SOHO) [1, 2] is a 3-year, prospective, observational study of antipsychotic treatment outcomes.

Remission was defined as I) achieving a level of severity of mild or less (<4 in a scale from 1 to 7) in the CGI positive, negative, cognitive, overall severity score that had been maintained for six months or longer, and ii) Not having any inpatient admission during that period.

A logistic regression model was used to analyse factors associated with remission.

Results: 10, 972 patients were enrolled and 6350 patients were included in the analysis; 4261 (67%) achieved remission. Paid employment (OR 1.49; 95% CI 1.31-1.69) was associated to achieving remission. Higher CGI severity at baseline (0.76; 0.70-0.82), and male gender (0.79; 0.71-0.87) were associated to lower frequency of remission. Taking Quetiapine (0.66; 0.56-0.76), Risperidone (0.74; 0.66-0.83), Oral Typicals (0.64; 0.55-0.74), Depot Typicals (0.59; 0.50-0.69) and Amilsupride (0.73; 0.56-0.94) was associated to a lower frequency of remission compared to patients starting Olanzapine. **Conclusions:** 23% of patients achieved remission. Employment status, lower clinical severity, female gender and treatment with Olanzapine were factors associated with remission.

References:

1. Haro JM, Edgell ET, Jones PB, Alonso J, Gavart S, Gregor KJ, Wright P, Knapp M, on behalf of the SOHO Study Group.

SOHO Study: rationale, methods and recruitment. Acta Psychiatrica Scandinavica 2003;107(3):222-32.

2. Haro JM, Edgell ET, Frewer P, Alonso J, Jones PB on behalf of the SOHO Study Group. The European Schizophrenia Outpatient Health Outcomes Study: baseline findings across country and treatment. Acta Psychiatr Scand 2003; 107 (Suppl 416):1-9.

NR414 Tuesday, May 23, 12:00 PM - 2:00 PM

Use of Long Acting Fluphenazine, Haloperidol or Risperidone in a Medicaid Population

Mark Olfson, M.D. *Columbia University, Psychiatry, 1051 Riverside Drive, New York, NY, 10032*, Haya Ascher-Svanum, Ph.D., Steven Marcus, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to describe the characteristics of patients with schizophrenia who start fluphenazine decanoate or enanthate, haloperidol decanoate, or long acting injectable risperidone.

Summary:

Background: Three long-acting injection antipsychotic medications are available in the US: fluphenazine decanoate or enanthate (FD), haloperidol decanoate (HD), and long acting injectable risperidone (LAR). Little is known about their use in community practice.

Objective: Compare patients with schizophrenia during the 6 month period preceding initiation of FD, HD, or LAR injections, focusing on patient characteristics related to medication non-adherence.

Method: An analysis was conducted of 2001-2004 California Medicaid (Medi-Cal) claims data of adults with schizophrenia ages 18 to 64 years. Comparisons are presented of patients who received one or more injection of FD (n=948), HD (n=1,631), or LAR (n=116) but no long-acting antipsychotic injections during the preceding 6 months.

Results: The three groups had a similar gender distribution (% male: FD: 59.5%, HD: 58.7%, LAR: 50.0%) (χ^2=3.9, df=2, p=.15), though they differed in mean age (FD: 41.2 years; HD: 39.9 years, LAR: 39.4 years, F=4.8, df=2/2,692, p=.009), and racial composition (% white: FD: 51.4%, HD: 44.7%, LAR: 48.3%) (χ^2=10.6, df= 2, p=.005). During the six months before the index injection, most patients in each group had oral antipsychotic medication possession ratios (MPR) below .80, indicating significant medication nonadherence (FD: 53.4%; HD: 58.6%, LAR: 61.2%) (χ^2=6.9, df=2, p=.03). During this period, the three groups did not significantly differ with respect to the proportion who received treatment of substance use disorders (FD:15.3%, HD:15.4%, LAR: 11.2%, χ^2= 1.5, df=2, p=.47), psychiatric emergency room visits (FD: 28.6%, HD: 28.8%, LAR: 28.4%, χ^2=.02, df=2, p=.99), or psychiatric hospital admissions (FD: 1.0%, HD: 1.6%, LAR: 0.9%, χ^2=2.1, df=2, p=.35). *Conclusions*: In the months before initiating each of the long-acting injection antipsychotic medications, most patients have evidence of non-adherence with oral antipsychotic medications, many use psychiatric emergency services, and some receive treatment for substance use disorders.

References:

1. West JC, Wilk J, Olfson M, Rae DS, Marcus S, Narrow WE, Pincus HA, Reiger DA: Patterns and quality of treatment of patients with schizophrenia in routine psychiatric practice. Psych Serv 2005; 56:283-291.

2. Rothbard AB, Kuno E, Roley K: Trends in the rate and type of antipsychotic medications prescribe to persons with schizophrenia. Schiz Bull 2003;29:531-40.

NR415 Tuesday, May 23, 12:00 PM - 2:00 PM

Weight Effects Associated With Ziprasidone Treatment: A Comphrensive Database Review

Bruce Parsons, M.D. *Pfizer Inc, CNS Psychiatry, 235 E 42nd St, NY, NY, 10017-5703*, Steve R. Murray, M.D., Earl Giller, Jr., M.D., Cynthia Siu, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participants will have a greater understanding of the long-term effects of ziprasidone on weight gain and loss.

Summary:

Introduction: Weight gain and obesity are linked to an increased risk for cardiovascular disease, diabetes and hypertension, and some antipsychotics produce weight gain.[1] We examined ziprasidone's clinical trial database to characterize weight change and to explore the relationship between weight change and dose, gender, and duration of ziprasidone treatment.

Methods: Post-hoc integrated analyses of 21 placebo-controlled studies were performed, consisting of 3946 subjects. Patients were classified into three groups: weight unchanged (within 7% of baseline), increased or decreased (>7% of baseline).

Results: In short-term studies, the majority of patients (80.8-88%) in each ziprasidone dose category were unchanged. There were few differences between the proportions of patients who lost (0.8-4.5%) and those who gained (11.2-14.7%) weight. In long-term studies, the weight change distribution was similar between the combined ziprasidone dose and placebo groups, with the majority of those with weight changes having lost weight. At 6 and 12 months, 50-63.4% patients remained unchanged, 23.6-41.2% had >7% weight loss, and only 3.7-16.4% had > 7% weight gain. Overall, there was no relationship between the distribution of weight change and ziprasidone dose, treatment duration, or gender.

Conclusion: This comphrensive analysis confirms that ziprasidone is associated with an overall weight neutral profile,[2] with some evidence for weight loss in long-term treatment.

References:

1. Allison DB, et al. Antipsychotic-Induced Weight Gain: A Comprehensive Research Synthesis. Am J Psychiatry. 1999; 156: 1686-1696.

2. 2Simpson GM, et al. Six-Month, Blinded, Multicenter Continuation Study of Ziprasidone Versus Olanzapine in Schizophrenia. Am J Psychiatry. 2005; 162: 1535-1538.

NR416 Tuesday, May 23, 12:00 PM - 2:00 PM

Reliability, Validity, and Sensitivity to Change of the Personal and Social Performance Scale in Patients With Acute Schizophrenia

Donald Patrick, Ph.D. *University of Washington, Health Services, Box 357660 1954 NE Pacific Street, Seattle, WA, 98195-7660*, PierLuigi Morosini, M.D., Margaret Rothman, Ph.D.

Educational Objectives:

At the conclusion of this presentation, participants should understand that the Personal and Social Performance scale is a reliable and valid measure of personal and social function in patients with acute schizophrenia with good construct validity and sensitivity to clinical change.

Summary:

Background: The Personal and Social Performance scale (PSP) has been shown to have good reliability and validity in patients with stabilized schizophrenia[1]. The PSP provides a single

composite rating that considers 4 domains of personal and social functioning (socially useful activities, relationships, self-care, aggressive behaviors) over a 1 month recall period. The objective of this research is to present data on validity, reliability, responsiveness and minimally important difference (MID) in patients with acute schizophrenia.

Method: Data from a cross-sectional validation study (n=299) and three pooled clinical antipsychotic trials (n=1692), including patients with acute psychotic symptoms (mean PANSS at baseline >90), were analyzed. Outcome measures included PANSS, CGI-S and PSP. Intraclass correlation coefficients (ICC) were derived to assess inter-rater and test-retest reliability. Convergent and discriminant validity, sensitivity of the PSP to clinical change and MID were evaluated.

Results: The test-retest and inter-rater ICCs exceeded 0.80, indicating good reliability. The PSP was more highly correlated with PANSS items expected to have an impact on social function (active social avoidance [ρ=-0.26], emotional withdrawal [ρ=-0.23], passive/apathetic social withdrawal [ρ=-0.24]). The PSP was able to discriminate between different levels of CGI severity ($p<0.005$). Regression analyses showed that the PSP is sensitive to change in PANSS total score ($p<0.0001$). Based on a 1 category improvement in CGI-S, the observed between-group MID for PSP in acute patients was 8 to 9 points.

Conclusions: These data support the PSP as a valid and reliable clinician-reported measure of personal and social function in patients with acute schizophrenia.

References:

1. Morosini PL et al.: Development, reliability and acceptability of a new version of the DSM-IV Social and Occupational Functioning Assessment Scale (SOFAS) to assess routine social functioning. Acta Psychiatr Scand 2000; 101(4):323-329.
2. Mueser KT, Tarrier N: Handbook of Social Functioning in Schizophrenia. Boston, Allyn and Bacon, 1998.

NR417 Tuesday, May 23, 12:00 PM - 2:00 PM

A Psychosis-Specific Quality of Life Scale (PSQOLS) for Schizophrenia

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Educational Objectives:

To help understanding the impact of schizophrenic illness on patient's quality of life

Summary:

Objective:

The objective of this study was to develop and validate a Psychosis-Specific Quality of Life Scale (PSQOLS), consisting of a questionnaire measuring issues related to patients with schizophrenia.

Method:

During a first phase, identical patterns were identified from interviews of patients (n=100) with schizophrenia (DSM-IV). Following a meeting with 25 experts to discuss the data obtained, the structure of the scale was formulated and included 133 items, taking 35-40 minutes for patients to complete. In a prospective study (n=686), a validation analysis of structural and psychometric properties was performed. Finally, test/retest reliability was assessed in 100 patients over a period of 7 days on the first and last days.

Results:

Data from 686 patients with schizophrenia were analyzed. Internal consistency analysis identified 14 factors (74 items) with a Cronbach alpha of 0.75 to 0.95. Construct validity was confirmed using the Brief Psychiatry Rating Scale (BPRS), the Clinical Global Impression (CGI) of Improvement Scale, the Psychological Aptitude Rating Scale (PARS), the Functional Status questionnaire (FSQ). Lastly, there was a high test/retest reliability for each factor ($p<0.001$).

Conclusion: The PSQOLS, a patient-oriented self-evaluation, is an efficient, multidimensional instrument designed to measure the impact of schizophrenia on quality of life.

References:

1. Heinrichs DW, Hanlon TE, Carpenter WT. The quality of life scale: an instrument for rating the schizophrenic deficit symptoms. Schizophrenia Bulletin. 1984; 10:388-398.
2. Auquier P, Simeoni MC, Sapin C, Reine G, Aghabadian V, Cramer J, Lançon C. Development and validation of a patient-based health-related quality of life questionnaire in schizophrenia: the S-QoL. Schizophrenia Research. 2003; 63:137-149.

NR418 Tuesday, May 23, 12:00 PM - 2:00 PM

Cognitive Remediation Therapy and Cognitive Behavior Therapy in Chronic Schizophrenia: Effects on Symptoms Cognition and Psychosocial Functioning

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Educational Objectives:

In the presentation different aspects of Cognitive Remediation Therapy in chronic schizophrenia, such as efficacy, effect sizes, and the impact on cognition, symtoms and psychosocial functioning will be disscussed taking into account the results of a randomized controlled study. A comparison against the effects of Cognitive Behavioral Therapy on the same population will shown some sort of specificity of the effects of both psychological therapies. A different group without any sort of psychological tretament will show that there is no practice effect of the neuropsychological test after using a Reliable Change Index. The positive resulta are maintained after a mothns follow-up.

Summary:

Objective: Cognitive Remediation Therapy (CRT) is a novel treatment based on the Extended Release rorless learning approach designed to improve adaptative functioning by using cognitive compensatory strategies to bypass the cognitive deficits associated with schizophrenia. The effect of this treatment was tested on neurocognition, symptomatology and psychosocial functioning. Cognitive Behavioural Therapy (CBT) is a useful treatment for emotional problems that is not expected to have effects on neurocognition and it was used as a control condition.

Method: A total of 40 chronic patients with DSM-IV schizophrenia disorder, cognitive impairments and prominent negative symptoms were randomly assigned for 4 months to one of the two treatment conditions: 1) standard medication plus CRT, 2) standard medication plus Cognitive-Behavior Therapy . Comprehensive assessments were conducted before and after the treatments (CRT or Cognitive-Behavior Therapy) and at the end of a follow-up period of 6 months. Additionally, a method to establish reliable change was calculated from the neurocognitive measures of a different sample of 20 schizophrenic patients who were under treatment as usual (TAU) condition: standard medication without any kind of psychological treatment.

Results: CRT has a specific treatment effect on Psychomotor Speed, Verbal and Non-verbal Memory, and Executive Function. Patients receiving CRT showed greater mean differences and

more large effect-size changes (Mean effect size = 0.5) than did patients receiving Cognitive-Behavior Therapy . Cognitive-Behavior Therapy only showed a little non-specific improvement in Working Memory. Patients receiving CRT achieved improvements in social functioning, showing that cognitive improvements are clinically meaningful. These gains were not vanished after the 6 month follow-up.

Conclusions: These results support the efficacy of CRT and it might be concluded that CRT is a useful treatment tool in targeting neurocognitive impairment because it increased neurocognitive functioning to a degree not achievable from the non-specific stimulation.

References:

1. Twanley EW, Jeste DW, Bellack AS: A review of cognitive training in schizophrenia. Schizophr Bull 2003; 29: 359-382.
2. Bark N, Revheim N, Huq F, Khalderov V, Ganz ZW, Medalia A: The impact of cognitive remediation on symptoms of schizophrenia. Schizophr Res 2003; 63: 229-235.

NR419 Tuesday, May 23, 12:00 PM - 2:00 PM

Remission Criteria for Schizophrenia Evaluated in a Large Naturalistic Cohort

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Educational Objectives:

The participant should understand the importance of the evaluation of the criteria for remission in patients with schizphrenia.

Summary:

Introduction: Recently, criteria for remission in schizophrenia have been proposed. Remission is defined by low symptom levels (PANSS score ≤ 3 on 8 core symptoms: delusions, hallucinations, unusual thought content, conceptual disorganisation, mannerisms/posturing, blunted affect, social withdrawal and lack of spontaneity) for at least 6 months.

Method: Remission criteria were evaluated in a large naturalistic cohort of schizophrenic patients (N = 909) who are prospectively being followed and assessed with PECC (Psychosis Evaluation tool for Common use by Caregivers, assessment of symptoms, side-effects, ADL, current treatments) in different Belgian treatment settings.

Results: Data were analyzed on 422 patients with a minimal follow-up of 1 year (multiple assessments, no medication change). 29% of these patients meet remission criteria at last observation.

Patients in remission compared, to patients not meeting remission criteria, have significant lower total symptom scores, better insight, better GAF- and lower CGI-scores (P = 0.0001). Patients in remission score significantly better in different functional domains (personal hygiene, household tasks, money matters, daily activities/work and social contacts) (P = 0.0001).

Conclusion: The remission concept is valid for daily clinical practice and could be an achievable goal for treatment in routine care.

NR420 Tuesday, May 23, 12:00 PM - 2:00 PM

Asenapine Safety and Tolerability During Acute Schizophrenia: A Placebo- and Risperidone-Controlled Trial

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to:

1. Compare the safety and tolerability profiles of asenapine and risperidone in patients with acute exacerbation of schizophrenia.
2. Assess the relative risks of extrapyramidal symptoms and weight gain with asenapine versus resperidone.

Summary:

Objective: To evaluate the safety and tolerability of asenapine, a novel psychopharmacologic agent, in patients with acute schizophrenia.

Methods: In a double-blind, multicenter trial, adult patients with acute exacerbation of schizophrenia were randomly assigned to 6 weeks of treatment with sublingual asenapine 5 mg BID plus oral placebo, oral risperidone 3 mg BID plus sublingual placebo, or double placebo BID. Adverse events and extrapyramidal symptoms (EPS) were assessed weekly and 30 days after study exit.

Results: Among 180 patients who received study medication (asenapine, n=59; risperidone, n=59; placebo, n=62), 151 (84%) had ≥1 adverse event. The most frequently reported events were headache and agitation (placebo and risperidone), followed by transient sleep disturbances (active medications). Although there were no significant between-group differences on formal ratings of EPS, hypertonia and hyperkinesia were more frequent with risperidone (12% and 7%, respectively) than with placebo (3%, 0%) or asenapine (0%, 0%), and concomitant use of antiparkinsonian drugs was more frequent with risperidone (31%) than with asenapine (17%). Clinically significant weight gain (≥7% increase in body weight) occurred more often with risperidone (17%) than with asenapine or placebo (4% and 2%; both $P<0.05$); mean weight gain was similar in all 3 treatment groups among normal-weight patients, but greater with risperidone among overweight patients. The incidence of hyperprolactinemia was higher with risperidone (79%) than with asenapine or placebo (9% and 2%; both $P<0.0001$). Changes in blood pressure and heart rate were comparably small in all 3 treatment groups, and there were no cases of QTc prolongation beyond 500 ms in any group.

Conclusions: Asenapine appears to be well tolerated by patients with acute schizophrenia, and is associated with low incidence rates of EPS, hyperprolactinemia, and clinically significant weight gain.

Funding Source: This study was supported by Organon USA Inc. and Pfizer Inc.

References:

1. Lehman AF, Lieberman JA, Dixon LB, McGlashan TH, Miller AL, Perkins DO, Kreyenbuhl J: Practice guideline for the treatment of patients with schizophrenia, second edition. Am J Psychiatry 2004; 161:1-56.
2. Leucht S, Wahlbeck K, Hamann J, Kissling W: New generation antipsychotics versus low-potency conventional antipsychotics: a systematic review and meta-analysis. Lancet 2003; 361:1581-1589.

NR421 Tuesday, May 23, 12:00 PM - 2:00 PM

Asenapine Efficacy for the Treatment of Acute Schizophrenia: A Randomized, Placebo- and Risperidone-Controlled Trial

Steven G. Potkin, M.D., Miriam Cohen, Ph.D., John Panagides, Ph.D., Anil S. Jina, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to compare the efficacy of asenapine versus risperidone and placebo in reducing the positive and negative symptoms of schizophrenia.

Summary:

Objective: Asenapine is a novel psychopharmacologic agent being developed for the treatment of schizophrenia and bipolar disorder. This double-blind trial evaluated the efficacy of asenapine vs placebo and risperidone in acute schizophrenia.

Methods: Patients with baseline Clinical Global Impression (CGI) score =4 and Positive and Negative Syndrome Scale (PANSS) total score =60 were randomized to sublingual asenapine 5 mg BID with oral placebo, oral risperidone 3 mg BID with sublingual placebo, or double placebo for 6 weeks. The primary efficacy parameter was change from baseline in PANSS total score for asenapine vs placebo. Secondary measures included changes in PANSS positive, negative, and general psychopathology subscale scores and CGI.

Results: There were 58, 56, and 60 patients in the asenapine, risperidone, and placebo groups, respectively. By week 6, mean change in PANSS total score was -15.2 with asenapine vs -4.3 with placebo ($P<0.005$); the change with risperidone was also greater than placebo (NS). Reductions in CGI were similar with asenapine and risperidone (-0.74 and -0.75, respectively; both $P<0.01$ vs placebo). Both active treatments were significantly ($P<0.05$) better than placebo in reducing PANSS positive subscale scores (-5.2, -2.3, and -4.7 for asenapine, placebo, and risperidone). On the PANSS negative subscale, change with asenapine (-3.1) was significantly greater than with placebo (-0.2, $P<0.01$) or risperidone (-0.9, $P<0.05$). On the PANSS general psychopathology subscale, change was -6.9 with asenapine vs -1.6 with placebo ($P<0.005$) and change with risperidone was also greater than placebo (NS). Both active treatments were well tolerated, although weight gain and hyperprolactinemia were more frequent with risperidone.

Conclusions: Asenapine is effective and well tolerated in the treatment of acute schizophrenia.

Funding Source: This research was supported by Organon Inc USA, Roseland, NJ and Pfizer Inc, New York, NY.

References:

1. Shahid M, Wong E: Asenapine has a unique human receptor binding signature. World J Biol Psychiatr 2005; 6:360.
2. Moller HJ, Bottlender R, Wegner U, Wittmann J, Strauss A: Long-term course of schizophrenic, affective and schizoaffective psychosis: focus on negative symptoms and their impact on global indicators of outcome. Acta Psychiatr Scand Suppl 2000:54-5.

NR422 Tuesday, May 23, 12:00 PM - 2:00 PM

Preferential Aggregation of Obsessive-Compulsive Spectrum Disorders in Schizophrenia Patients with OCD

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Educational Objectives:

At the conclusion of this presentation, the participants will appreciate the rate and pattern of additional psychiatric co-morbidity in schizophrenia patients with obsessive-compulsive disorder (OCD) and to make comparisons with non-OCD schizophrenia and pure OCD patients. Specifically there is a preferential aggregation of OCD spectrum disorders; body dysmorphic disorder, eating disorders, and chronic tic disorders in schizo-obsessive patients. Identification of these co-morbid conditions may improve the diagnostic validity of a schizo-obsessive subgroup in schizophrenia.

Summary:

Objective: To further validate the existence of a complex schizophrenia - OCD association, we evaluated the rate of OCD-spectrum and additional Axis I psychiatric disorders in schizo-obsessive patients, as compared to non-OCD schizophrenia and "pure" OCD patients.

Method: A consecutive sample of 100 patients who met DSM-IV criteria for both schizophrenia and OCD (N = 100) were compared with non-OCD schizophrenia patients (N = 35, OCD) and healthy controls (N = 161), matched for age and number of hospitalizations. Structured Clinical Interview for DSM-IV Axis I disorders was used. OCD-spectrum disorders included BDD, chronic tic disorders, eating disorders and hypochondriasis.

Results: There was a robust between-group difference in the number of patients with at least one OCD-spectrum disorder (schizo-obsessive 30 versus schizophrenia 8; OR = 4.35; 95% CI = 2.13 to 11.41; p = .001), accounted for by the substantially higher rate of BDD (8% versus 0) and chronic tic disorders (16% versus 4%) in the schizo-obsessive group. Two OCD-spectrum disorders were found in 8/100 schizo-obsessive patients and none in the schizophrenia group (p = .0039). No significant between-group difference was revealed in the rate of affective, anxiety and substance use disorders. There was a comparable rate of OCD-spectrum disorders in the schizo-obsessive and OCD groups (30% and 42.8%, p = .32).

Conclusion: Preferential aggregation of OCD-spectrum disorders in the schizo-obsessive group supports the validity of this unique clinical association. Whether OCD in schizophrenia represents comorbidity or a specific schizo-obsessive subtype of schizophrenia warrants further investigation.

References:

1. Poyurovsky M, Kriss V, Weisman G, et al. Comparison of clinical characteristics and comorbidity in schizophrenia patients with and without OCD: schizophrenic and OC symptoms in schizophrenia. J Clin Psychiatry. 2003; 64:1300-1307.
2. Poyurovsky M, Kriss V, Weisman G, et al. Familial aggregation of schizophrenia-spectrum disorders and obsessive-compulsive associated disorders in schizophrenia probands with and without OCD. Am J Med Genet B Neuropsychiatr Genet. 2005;133:31-36.

NR423 Tuesday, May 23, 12:00 PM - 2:00 PM

Obesity and Health-Related Quality of Life in Swedish Patients With Schizophrenia.

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Educational Objectives:

The presentation will give additional insight to the importance of adressing weight gain and obesity in patients with psychotic illness.

Summary:

Introduction:

Weight gain and obesity-related health problems cause increased morbidity in patients with psychotic disorders. Previous data indicate reduced self-reported quality of life in patients with schizophrenia and population surveys indicate reduced quality of life in obesity. The purpose of this study was to examine the impact of weight gain and obesity on health related quality of life (HRQL) in schizophrenia.

Methods:

The study was performed as part of a prospective cross-sectional study of metabolic risk factors in Swedish patients with psychotic illness. Body weight and height were measured and BMI (body mass index) calculated. All subjects filled in questionnaires including EQ5D, a validated HRQL instrument. Self reported weight change since commencement of antipsychotic treatment was noted. The results were compared to a population based survey with self-reported body height, weight and EQ5D from 29.000 subjects.

Results:

Data from 220 consecutive patients included in the study: 70% of the females and 80 % of the males have a BMI > 25 kg/m2 and 35% are obese, compared with 35% (female) and 50% (male) overweight and 10% obese in the population sample. 50% of the patients report weight gain of 10kg or more since antipsychotic treatment was started. Self reported quality of life was reduced in schizophrenia, with negative impact of increasing body mass. The effect of the mental disorder on HRQL was more pronounced in males than females. However, subjects reporting weight loss since start of treatment had a lower EQ5D score than those reporting moderate weight gain.

Discussion:

The study confirms previous data on the high prevalence of obesity in this patient population. The negative effect of obesity is additive to the negative effect of the mental disorder on self-reported health-related quality of life.

References:

1. Jia H: The impact of obesity on health-related quality-of-life in the general adult US population. J Public Health 2005; 27(2):156-64.
2. Prieto L: Psychometric validation of a generic health-related quality of life measure (EQ-5D) in a sample of schizophrenic patients.

NR424 Tuesday, May 23, 12:00 PM - 2:00 PM

Long-Acting Risperidone Treatment Following Antipsychotic Polypharmacy

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand the scope of antipsychotic polypharmacy, its association with compliance problems, and the efficacy and safety of long-acting risperidone maintenance therapy in patients previously managed with antipsychotic polypharmacy.

Summary:

Objective: To examine long-acting, injectable risperidone maintenance treatment in stable patients with schizophrenia or schizoaffective disorder previously managed with antipsychotic polypharmacy. Polypharmacy can be associated with refractory illness or suboptimal response. In cases of poor compliance, assured medication delivery with a long-acting agent may be helpful.

Methods: A post-hoc analysis was completed of a double-blind study in which stable patients were randomized to long-acting risperidone 25 or 50 mg every 2 weeks for 52 weeks. Polypharmacy was defined as patients receiving more than one antipsychotic agent at study entry. Outcomes included relapse, the Positive and Negative Syndrome Scale (PANSS), Clinical Global Impressions of Severity and adverse-event reports.

Results: Seventy-three of the 323 patients (22.6%) were receiving antipsychotic polypharmacy at study entry. Relapse incidence in this subpopulation was 28.8%, with psychiatric hospitalization reported as the reason for relapse in 8.2% of patients, change in PANSS total score in 4.1%, change in CGI score in 11.0%, and rescue medication in 5.5% of patients. Results were similar with the 25- and 50-mg doses of long-acting risperidone. The mean ± SD PANSS total score reflected symptom stability during the trial: 69.4 ± 17.7 at baseline and 67.0 ± 18.6 at endpoint (P = 0.291). The most common adverse events in this subpopulation were: insomnia (37%), psychotic disorder not otherwise specified (27%), anxiety (21%), headache (10%), and tremor (10%).

Conclusions: In patients previously receiving antipsychotic polypharmacy, long-acting risperidone was associated with a high proportion of patients who remained out of the hospital (91.8%) and relapse free (71.2%).

Supported by Janssen, LP.

References:

1. Ganguly R, Kotzan JA, Miller LS, Kennedy K, Martin BC: Prevalence, trends, and factors associated with antipsychotic polypharmacy among Medicaid-eligible schizophrenia patients, 1998-2000. J Clin Psychiatry 2004; 65:1377-1388.
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NR425 Tuesday, May 23, 12:00 PM - 2:00 PM

Comparative Efficacy and Safety of Ziprasidone and Clozapine in Treatment Refractory Schizophrenic Patients: Results of a Randomized, Double-Blind, 18-Week Trial

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Educational Objectives:

The research data presented will contribute to the participant's understanding of the safety and efficacy of difficult to manage patients diagnosed with schizophrenia who do not respond and/or are intolerant of antipsychotic treatment.

Summary:

Objective: To evaluate the efficacy and safety of ziprasidone and clozapine in refractory schizophrenic patients.

Methods: Patients were enrolled who met criteria for treatment resistance (non-response in >3 adequate trials in past 5 years) and/or inability to tolerate antipsychotic treatment; and who had a PANSS>80. Patients completed a 3-7 day screening period before being randomized, double-blind, to 18 weeks of parallel-group treatment with either ziprasidone (80-160 mg/day; n=73) or clozapine (250-600 mg/day, n=74).

Results: On the primary ITT-LOCF analysis, the baseline-to-endpoint decrease in PANSS total score was similar for ziprasidone (-25.0 ± 22.0; 95% CI: -30.2 to -19.8) and clozapine (-24.5 ± 22.5; 95% CI: -29.7 to -19.2). A significant reduction from baseline in the PANSS total score was observed from the first visit at day 11 for both ziprasidone ($p < 0.001$) and clozapine ($p = 0.003$) and at all subsequent post-baseline visits. The mean endpoint improvement was also similar on the CDSS, the CGI-I, and GAF. There were fewer treatment-related adverse events, and a more favorable metabolic profile for ziprasidone: significant ($p<0.05$) reduction in median cholesterol (-5 versus +2 mg/dL), LDL cholesterol (-6 versus +4 mg/dL), and triglycerides (-15 versus +10 mg/dL); no change in fasting glucose (0 versus +6 mg/dL), and significantly less weight gain ($p<0.001$).

Conclusion: In this treatment-resistant/intolerant patient sample, ziprasidone demonstrated comparable efficacy but increased tolerability and metabolic safety when compared to clozapine.

References:

1. 1. Conley RR, Buchanan RW. Evaluation of treatment-resistant schizophrenia. Schizophr Bull 1997;23:663-674.

2. 2. Nemeroff CB, Masand PS, Lieberman JA, Weiden PJ, Harvey PD, Newcomer JW, Schatzberg AF, Kilts CD, Daniel DG. From Clinical Research to Clinical Practice: A 4-Year Review of Ziprasidone. CNS Spectr 2005;10 Suppl 17:1-19.

NR426 Tuesday, May 23, 12:00 PM - 2:00 PM

Genetic Association Analysis Between the hOGG1 Gene Polymorphism (Ser326Cys) and Schizophrenia

Shinichi Sakata *University of Occupational and Environmental Health, 1-1 Iseigaoka, Yahatanishi-ku, Kitakyushu, 807-8555, Japan*, Takahiro Shinkai, Hiroko Hori, Osamu Ohmori, Jun Nakamura

Educational Objectives:

At the conclusion of this presentation, the participant should be able to demonstrate clinical implications.

Summary:

Rationale: DNA is damaged by a variety of agents including oxidative stress caused by reactive oxygen species (ROS) derived from oxidative metabolism. Oxidative stress such as free radical-mediated neuronal dysfunction may be involved in the pathophysiology of schizophrenia. The human 8-oxoguanine DNA glycosylase (hOGG1) plays an important role in the repair of damaged DNA. We therefore hypothesized that the hOGG1 gene, which is located on chromosome 3p26.2, may be involved in the pathophysiology of schizophrenia. The aim of this study is to examine whether a functional polymorphism, a serine (Ser) to cysteine (Cys) substitution at codon 326 (Ser326Cys) of the hOGG1 gene, is associated with susceptibility to schizophrenia in a Japanese case-control sample. It is reported that the potential capacity of hOGG1 with the 326Ser to repair the damaged DNA is ~7 times higher than that with the 326Cys, suggesting that 326Cys allele may give an individual more susceptibility to the formation of 8-hydroxyguanine in DNA. *Material and Methods*: Our sample includes 240 patients with schizophrenia (DSM-IV) and 198 normal controls. Informed consent was a premise for participation, and this study was approved by the Ethics Committee of the University of Occupational and Environmental Health. Genomic DNA was extracted from 10-ml aliquots of EDTA-anticoagulated venous blood following the standard procedures. Genotyping was assessed by the TaqMan allele-specific assay method using ABI PRISM® 7000 (Applied Biosystems) at the Bio-information Research Center, University of Occupational and Environmental Health. Differences in allele and genotype distribution between cases and controls were evaluated using the χ^2 test. *Results*: Significant association between the hOGG1 Ser326Cys polymorphism and schizophrenia was found (genotype: $\chi^2 = 6.04$, df = 2, $p = 0.049$). *Conclusion*: Our results suggest that the hOGG1 Ser326Cys polymorphism may confer susceptibility to schizophrenia in our sample.

References:

1. CNS Drugs. 2001;15(4):287-310.

2. Nutr Neurosci. 2002 Oct;5(5):291-309.

NR427 Tuesday, May 23, 12:00 PM - 2:00 PM

Immigration and Demographic Variables as Predictors of Long-Term Outcome in Schizophrenia

Nandita Sawh *York University, 129 Derrydown Road, North York, ON, M3J 1R6, Canada*, R. Walter Heinrichs, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand that demographic and immigration-related factors may play noteworthy roles in the varying degrees of long-term functional outcome observed in persons diagnosed with chronic schizophrenia

Summary:

Schizophrenia rates may be elevated within some immigrant populations in several countries. Migration to a new country may involve stresses like financial adversity and cultural adjustment. Moreover, these stresses may in turn yield poorer functional outcomes in foreign-born schizophrenia patients, relative to native-born ones. The present study used multiple regression to investigate whether demographic and immigration variables predict long-term functional outcome. Archival data from 49 chronic schizophrenia patients assessed during the 1990's were examined. The SIP (Sickness Impact Profile) and amount of total hospitalization were used as outcome measures. The SIP reflected illness adjustment and life quality and total duration of hospitalization was an indicator of "objective" functional outcome. The Brief Psychiatric rating Scale (BPRS) was employed as an indicator of psychopathology present at the time of testing. Results yielded a regression equation including gender, parental socioeconomic status, and patient's status as either foreign-born or native-born that predicted significant amounts of outcome variance. At the same time, having English as a first language did not contribute uniquely to prediction. The finding that place of birth varies with functional outcome in an illness that strikes young adults implies a role for immigration-linked experiences such as social adversity and cultural adjustment.

References:

1. Mortensen PB, Cantor-Graae E, McNeil TF, Pedersen, CB: Migration as a risk factor for schizophrenia: a Danish population-based cohort study. Br J Psychiatry 2003; 182:117-122.

2. Perlick D, Stastny P, Mattis S, Teresi J: Contribution of family, cognitive and clinical dimensions to longterm outcome in schizophrenia. Schizophr Res 1992; 6:251-265.

NR428 Tuesday, May 23, 12:00 PM - 2:00 PM

Functional Polymorphism of the Human Multidrug-Resistance Gene (MDR-1) and Polydipsia-Hyponatremia in Schizophrenia

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to demonstrate clinical implications.

Summary:

Rationale: P-glycoprotein, which is coded by MDR-1 gene, in the brain capillary endothelial cell limits the entry of many drugs including antipsychotics into the brain. The aim of this study is to examine whether a functional polymorphism, a C to T substitution at position 3435 in exon 26 of the MDR-1 gene, is associated with susceptibility to polydipsia-hyponatremia in schizophrenia in a Japanese case-control sample. It has been reported that individ-

uals homozygous for this polymorphism had significantly lower duodenal MDR-1 expression levels and function of MDR-1 (PNAS, 97: 3473-3478, 2000). Furthermore, the brain entry of risperidone and 9-hydroxyrisperidone has been shown to be greatly limited by P-glycoprotein (Int J Neuropsychopharmacol, 7: 415-419, 2004). To our knowledge, this is the first association study between the MDR-1 polymorphism and polydipsia-hyponatremia in schizophrenia. *Material and Methods*: Our sample includes 331 patients with schizophrenia (DSM-IV) (84 with polydipsia and 247 without polydipsia). Informed consent was a premise for participation, and this study was approved by the Ethics Committee of the University of Occupational and Environmental Health. Genomic DNA was extracted from 10-ml aliquots of EDTA-anticoagulated venous blood following the standard procedures. Genotyping was assessed by the TaqMan allele-specific assay method using ABI PRISM® 7000 (Applied Biosystems) at the Bio-information Research Center, University of Occupational and Environmental Health. Differences in allele and genotype distribution between cases and controls were evaluated using the χ^2 test. *Results*: Significant association between the MDR1 C3435T polymorphism and polydipsia was found ($\chi^2 = 4.43$, df = 1, $p = 0.035$; OR = 1.46; 95%CI = 1.03-2.07). *Conclusion*: Our results suggest that the MDR1 C3435T polymorphism may confer susceptibility to polydipsia in schizophrenia.

References:

1. PNAS, 97, 3473, 2000.
2. Int J Neuropsychopharmacol, 7, 415-419, 2004.

NR429 Tuesday, May 23, 12:00 PM - 2:00 PM

Prodromal Symptoms in Late Adolescence

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Educational Objectives:

The objectives of this presentation is to identify symptoms which may be more prevalent in prodromal adolescents compared to controls. At the same time the participants will realize that many persons with first episode psychisis do not seek treatment for prodromal symptoms.

Summary:

Background: Although patients in their first psychotic episode suffer from prodromal behavioral disturbances, the nature of these disturbances is not yet well characterized defined.

Methods: We identified 59 soldiers (50m, 9f, ages 18-21, cases) later hospitalized for a psychotic disorder during their military service, who had been interviewed by a mental health professional within a 6 month period before being hospitalized. Soldiers who were found to be psychotic and were hospitalized as a result of the interview were excluded. The results of their mental health interview were compared to those of controls matched for age and gender who were not later hospitalized.

Results: Mild thought disorder (11.9% versus 2.3%, p<0.001), poor judgment (3.4% versus 0.7%, p<0.012), aggressive behavior (0% versus 5.7%, p=0.073) and obsessive-compulsive behavior (10.7 versus 2.7, p<0.001) were more common in cases compared with controls.

Discussion: In line with other data on the topic, these findings indicate that prodromal symptoms are non-specific and do not enable prediction of impending psychosis.

References:

1. Häfner H, Maurer K, Löffler W, an der Heiden W, Munk-Jørgensen P, Hambrecht M, Riecher-Rössler A: The ABC Schizophrenia Study: a preliminary overview of the results. Soc Psychiatry Psychiatr Epidemiol 1998; 33:380'386.
2. McGorry PD, Yung AR, Phillips LJ. The "close-in" or ultra high-risk model: a safe and effective strategy for research and clinical intervention in prepsychotic mental disorder. Schizophr Bull. 2003;29(4):771-90.

NR430 Tuesday, May 23, 12:00 PM - 2:00 PM

Community Screenings for Depression and Cognitive Decline

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that community screenings identify people suffering from depression and cognitive decline. Ways to improve compliance with follow up for subsequent care require further exploration.

Summary:

Objective:

Evaluate effectiveness of community screenings for identification of patients with depression and cognitive decline and referral of subjects to the appropriate sources of care.

Method:

18 older adults were evaluated during Screening Day offered by University of Massachusetts Memorial Health Care/Clinton Hospital geriatric psychiatry program. Mini Mental Status Exam (MMSE) and Geriatric Depression Scale (GDS) were administered, clinical assessment performed by geriatric psychiatrist and appropriate referrals given. Telephone follow up was done in to identify compliance with recommendations.

Results:

GDS scores and clinical evaluation indicated that 64% of subjects had no depression, 29% mild depression and 7% severe depression. Referrals to psychiatry outpatient clinic were made. Follow up called revealed that 60% of the referred subjects were not able to recall what was advised though only 20% had problems with recall on MMSE. 20% vaguely remembered advice but didn't follow up. Those displayed attention problems on MMSE. Only 20% scheduled appointment. 29% scored 30/30 on MMSE and clinical evaluation warranted no further intervention. 21% got 30/30 but appropriate referrals were made because of assessment findings required further exploration. 38% scored 28-29/30, 7% - 23/30, 7% - 14/30 and were all referred to memory clinic/outpatient psychiatry. On the follow up 50% didn't recall what was advised though only 30% has problems with recall on MMSE. 30% recalled that they were advised to see a doctor but 20% didn't make an appointment, 10% intended to make to follow up. Only 10% did actually make an appointment.

Conclusions:

Community screenings effectively identify target population. Ways to improve compliance with recommended interventions need to be further explored.

References:

1. Finifter DH, Jensen CJ, Wilson CE, Koenig BL: A comprehensive, multitiered, targeted community needs assessment model: methodology, dissemination, and implementation. Fam Community Health 2005; 28(4):293-306.
2. Manthorpe J, Iliffe S: Depression in Later Life. Philadelphia, PA, Jessica Kingsley Publishers, 2005.

NR431 Tuesday, May 23, 12:00 PM - 2:00 PM

Quetiapine Versus Olanzapine for the Treatment of Negative Symptoms in Patients With Schizophrenia

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Educational Objectives:

This study supports the effectiveness of quetiapine and olanzapine in treating the negative symptoms of schizophrenia.

Summary:

Negative symptoms are considered the most debilitating and refractory aspect of schizophrenia, being associated with poor social, occupational and global outcomes. Conventional antipsychotics have limited efficacy against these symptoms and poor tolerability profiles. Atypical antipsychotics are an alternative treatment, and this 12-Week, randomized, flexibly dosed study compared the efficacy, safety and tolerability of quetiapine and olanzapine in this regard. Of the 40 patients who entered the study (32 male: 8 female), 19 were randomized to quetiapine (mean dose 637 mg/day, mean treatment duration 80 days) and 21 to olanzapine (mean dose 16 mg/day, mean treatment duration 78 days). Quetiapine and olanzapine were similarly effective: in each treatment group, significant improvements at Week 12 were observed for the negative symptom scores on the Positive and Negative Syndrome Scale and for the subscale scores of affective flattening and alogia on the Scale for the Assessment of Negative Symptoms. Both treatments were also well tolerated in this patient population, with no worsening of extrapyramidal symptoms in either case. Anxiety and insomnia were the most common adverse events (≥7% of patients in each group), but were not drug-related. This study supports the effectiveness of quetiapine and olanzapine in treating the negative symptoms of schizophrenia.

References:

1. Reidel M,Moller H-J, Strassing M, et al. Efficacy of quetiapine versus risperidone in the treatment of schizophrenia with predominantly negative symptoms.Eur Psychiatry 2004b; 19(Suppl 1):90s, abs S44.05.
2. Tandon R. Direct effect of quetiapine on the negative symptoms of schizophrenia.Poster presented at the 155th Annual Meeting of the American Psychiatric Association, Philadelphia,USA,18-23 mAY,2002.

NR432 Tuesday, May 23, 12:00 PM - 2:00 PM

The First 21-Months of Safety Experience with Post-Marketing Use of Olanzapine's Intramuscular Formulation

Sebastian Sorsaburu, M.D. *Eli Lilly and Company, Lilly Research Laboratories, Lilly Corporate center, Indianapolis, IN, 46285*, Kenneth Hornbuckle, Ph.D., Debbie S. Blake, B.S., Debbie Falk, B.S., Mary Anne Dellva, M.S., Ludmila Kryzhanovskaya, M.D., Patrizia A. Cavazzoni, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant will be better informed about the adverse events reported during treatment with olanzapine IM.

Summary:

Objective: Severe agitation is common in patients with psychiatric disorders, often requiring the use of intramuscular (IM) medications. Data from the first 21 months of postmarketing safety experience with olanzapine IM are presented.

Methods: Lilly's safety database was searched for spontaneous adverse events (AEs) reported through September 30th, 2005.

Results: The estimated worldwide patient exposure to olanzapine IM was 539,000; 160 cases were reported. The most frequent reported underlying conditions included schizophrenia (34%), bipolar disorder (24%), psychosis (11%), dementia (9%), and depression (6%). The most common reported concomitant medications were benzodiazepines (29%) and other antipsychotics (54%). The most frequent AEs reported included CNS (21%), cardiac (12%), respiratory (6%), vascular (6%), and psychiatric (5%). There were 29 fatalities reported. These cases presented with multiple concomitant medications, including benzodiazepines (66%) or other antipsychotics (66%). The primary events reported in these cases included cardiovascular (41%), respiratory (21%), general (17%), and CNS (10%). The majority of the cases presented with medically significant risk factors.

Conclusions: Given the known challenges associated with the management acute agitation, clinicians should use care when treating these patients, who may present with concurrent medical conditions and may be treated with multiple medications.

References:

1. Waddington J.L.,Youssef, H.A, Kinsella, A. (1998). Brit J Psych, 173, 325-29.
2. Battaglia J. (2005). Pharmacological management of acute agitation. Drugs, 65, 1207-1222.

NR433 Tuesday, May 23, 12:00 PM - 2:00 PM

Factors Associated With Positive Outcomes for Homeless Men With Mental Illness

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Educational Objectives:

At the conclusion of this presentation, participants should be able to:

1. Describe an innovative model of service delivery to homeless individuals with complex health needs.
2. Appreciate the factors limiting the evaluation of shelter based interventions for the homeless.
3. Discuss the implications for program planning and policy development of the evaluation of a shelter based collaborative care team.

Summary:

Objective: Factors associated with positive outcomes for homeless men referred to a shelter based, collaborative care team were examined.

Methods: A chart review of 73 clients referred by shelter staff to our team over twelve months was completed. The two main outcome measures were clinical status and housing status six months after referral to the program.

Results: Fifty clients (68%) had a severe and persistent mental illness. Six months after referral, 24 clients (33%) had improved clinically and 33 (45%) were housed. Controlling for education, the presence of personality disorder, substance use disorders, treatment adherence, the number of psychiatric visits and the number of family physician visits, logistic regression identified two factors associated with positive housing outcomes: the number of psychiatric visits and treatment adherence. The same two variables were associated with clinical improvement.

Conclusion: Strategies to improve treatment adherence and access to mental health specialists may improve outcomes for the homeless mentally ill. In a healthcare system where mental health resources are scarce, a shelter-based collaborative care team is one possible solution.

References:

1. Dickey R: Review of programs for persons who are homeless and mentally ill. Harvard Rev Psychiatry 2000,8:242-250,.
2. Ambrosio E, Baker D, Crow C, et al: The Street Health Report: a study of the health status and barriers to health of homeless women and men in the City of Toronto. Toronto 1992.

NR434 Tuesday, May 23, 12:00 PM - 2:00 PM

Aripiprazole for the Treatment Of Schizophrenia With Co-Morbid Social Anxiety: Preliminary Findings From the Extension Phase Study

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that:

a. Social anxiety is a common comorbid condition in neuroleptic treated out-patients with schizophrenia.

b. Neuroleptic switch over to aripiprazole significantly reduced social anxiety, and psychosis severity, and improved quality of life over an eight-week course of treatment in this group of patients.

c. Schizophrenia patients with comorbid social anxiety who continued treatment with aripiprazole for up to one year maintained significant improvements from baseline in measures of social anxiety, and psychosis severity as well as quality of life throughout the treatment period.

d. Further controlled studies are warranted to confirm the efficacy of aripiprazole in the treatment of patients with schizophrenia and comorbid social anxiety.

Summary:

Background: Co-occurring social anxiety in patients with schizophrenia is common and often severe (1). 5-HT1A - receptor agonists such as aripiprazole are believed to be effective anxiolytic drugs (2). In an ongoing open-label study we tested the hypothesis that switchover to aripiprazole would reduce the severity of social anxiety in neuroleptic treated patients suffering from schizophrenia with co-morbid social anxiety. We present here the preliminary findings from 9 analyzable patients who entered the extension phase [EP] of the study.

Objectives: The EP hypothesized that switch-over to aripiprazole effectively reduces social anxiety symptoms in the short-term and that treatment continuation will help maintains the effects as assessed on the Liebowitz Social Anxiety Scale (LSAS), Sheehan's Disability Scale- [SDS] and Lehman's Quality of Life Interview [B-QOLI]- brief version.

Study Design: Eligible consenting outpatients meeting DSM IV criteria for schizophrenia or schizoaffective disorder with comorbid social anxiety symptoms completed baseline assessments after which their neuroleptic was gradually cross-titrated over to a maximum of 30 mg/po/day of aripiprazole. Patients who completed the 8-week acute study had the option to continue for 10 more months in the EP. Complete assessments were performed at day 56 and at months 4,6,9,and 12.

Results: Preliminary LOCF analysis of 9 patients showed significant improvements from baseline to day 56 and from baseline to month 12 in social anxiety scores (LSAS total, avoidance, and anxiety), social disability scores (Sheehan total, work, social life, family) and in overall function and emotional well being scores [B-QOLI.] and psychosis (PANSS total) scores.

Conclusions: These preliminary data suggest that switchover to aripiprazole improves acutely as well as in the long-term social anxiety, psychosis and quality of life in these patients. Further controlled studies are warranted.

Supported by a grant from Bristol-Myers Squibb, Investigator-Sponsored Trials Program .

References:

1. Pallanti S, Quercioli L, Hollander E.: Social anxiety in outpatients with schizophrenia: a relevant cause of disability. Am J Psychiatry. 2004 Jan;161(1):53-8.
2. Sramek JJ, Zarotsky V, Cutler NR.: Generalised anxiety disorder: treatment options. Drugs. 2002;62(11):1635-48.

NR435 Tuesday, May 23, 12:00 PM - 2:00 PM

A One-Year Follow-Up of Weight Gain in First-Break Psychotic Patients and Medication-Free Controls

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to distinguish between weight gain liabilities of various neuroleptic medications in the first-break psychosis patient population.

Summary:

Objective: BMI of patients suffering from schizophrenia exceeds that of population estimates. Most study samples include a high proportion of patients with chronic schizophrenia. We examined the extent of weight gain introduced after initiation of pharmacological treatment in previously drug-free first-episode psychotic patients, thereby possibly limiting various confounding variables such as multiple past medication trials, history of partial adherence; or poor diet and a sedentary lifestyle associated with chronic mental illness.

Methods: First-episode psychotic subjects receiving antipsychotics along with medication-free age- and gender-comparable control subjects were observed over a 1-year time frame. Main outcome measure was the BMI difference. Exploratory data analysis was conducted to account for possible inter-individual and group differences. Proportions of patients gaining a clinically significant amount of more than 7% over baseline weight were calculated.

Results: The sample consisted of 59 first-break psychosis patients at least 18 years old and 26 age- and gender comparable healthy controls (baseline BMI 24.1±5.1 versus 25.7±4.6; p=ns). At 1-year follow-up, patients had gained significantly more weight than controls (BMI +2.3±3.4 versus +0.4±1.6; p=0.007). Younger patients gained more weight (r=-0.302, p=0.020). 77.8 % of patients on Olanzapine (n=9; mean BMI increase +4.9±5.2); 54.2 % of patients on Risperidone (n=25; BMI +2.5±3.3); 44.4 % of those receiving Haloperidol (n=18, BMI 1.5±2.5); 14.3 % of the Perphenazine-treated patients (n=7; BMI 0.7±1.3); and 23.1 % of controls (n=26; BMI +2.3±3.4) gained more than 7 % of baseline bodyweight over a year.

Discussion: A high proportion of patients had gained more than 7 % over baseline BMI. Differential contributions of the various antipsychotics prescribed were observed. Long-term metabolic side-effects are numerous and may proportionally increase with BMI. The first treatment intervention is a critical step that has the potential to influence the course and outcome of what could become a lifelong illness.

References:

1. Haddad P. Weight change with atypical antipsychotics in the treatment of schizophrenia. J Psychopharmacol 2005; 19(6 Suppl):16-27.

2. Henderson DC. Schizophrenia and comorbid metabolic disorders. J Clin Psychiatry 2005; 66 Suppl 6:11-20.

NR436 Tuesday, May 23, 12:00 PM - 2:00 PM

Cardiac Risk Factors and Schizophrenia: An Analysis of 14,756 Patients Enrolled in an International, Comparative Trial of Olanzapine and Ziprasidone

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to: (1) understand the large simple trial (LST) design of the Ziprasidone Observational Study of Cardiac Outcomes (ZODIAC), a randomized, comparative study of ziprasidone and olanzapine, unprecedented in size and scope, being conducted among 18,000 patients with schizophrenia from 18 countries; (2) appreciate why the LST design was chosen to study ziprasidone cardiovascular safety; and (3) observe the baseline demographic and clinical characteristics of patients participating in ZODIAC, which intended to enroll subjects representative of the schizophrenia population.

Summary:

Introduction. Ziprasidone has been used to treat schizophrenia since 2000. An outstanding question has been whether its modest QTc-prolonging effect translates to increased risk of cardiovascular events. The Ziprasidone Observational Study of Cardiac Outcomes (ZODIAC), an open-label, randomized, postmarketing study, has been conducted to address this issue; it will complete enrollment of 18,000 schizophrenic patients from 18 countries in February 2006. The primary endpoint of non-suicide death will be ascertained over the following year.

Objective. To describe baseline characteristics of patients with schizophrenia enrolled from a variety of psychiatry practice settings in this large simple trial.

Methods. A physician-administered questionnaire collected baseline information on demographics, medical and psychiatric history, and concomitant medication use. Data were self-reported by patients or reported by enrolling physicians in naturalistic practice. Descriptive baseline data on 14,756 patients are presented here and will be updated following enrollment completion.

Results. To date, ZODIAC has enrolled over 17,000 patients. Most patients (81.5%) were from the U.S. or Brazil, baseline mean age was 41.9 years, 54.9% were male, and 61.2% were white. Nineteen percent of patients had hypertension, 15.7% had hyperlipidemia, 47.5% currently smoked, nearly two-thirds had a body mass index of 30 kg/m2 or more, and 8.3% had diabetes at baseline. Mean time since schizophrenia diagnosis was 10.8 years and average Clinical Impression Score was 5.1 (range: 1 to 8). One-third of patients had ever attempted suicide. Seventy-one percent of patients were using antipsychotics at baseline. Nearly 80% of patients were using concomitant medications, with 31.5% using antidepressants, 25.2% using anxiolytics, and 19.8% using mood stabilizers. Less than 3% were using antihypertensives or statins.

Conclusions. ZODIAC baseline data suggest that this study population has a substantial prevalence of cardiovascular risk factors. Concomitant medications were used frequently, although hyperlipidemia and hypertension may be undertreated.

Supported by funding from Pfizer

References:

1. Harrigan EP, Miceli JJ, Anziano R, Watsky E, Reeves KR, Cutler NR, Sramek J,.
2. March JS, Silva SG, Compton S, Shapiro M, Califf R, Krishnan R: The case for.

NR437 Tuesday, May 23, 12:00 PM - 2:00 PM

Effectiveness of Atypical Antipsychotics for Substance Abuse in Schizophrenia Patients

Jeffrey W. Swanson, Ph.D. *Duke University, Department of Psychiatry and Behavioral Sciences, DUMC Box 3071, Durham, NC, 27710*, Marvin S. Swartz, M.D., Richard A. Van Dorn, Ph.D.

Educational Objectives:

Participants should become familiar with new evidence for:
(1) Prevalence and risk factors for substance abuse in persons with schizophrenia in community-based treatment;
(2) Effectiveness of treatment with atypical antipsychotics and conventional neuroleptics in reducing substance abuse among patients with schizophrenia;
(3) Role of improved adherence with medication in reducing risk factors for substance abuse.

Summary:

Objectives: This study compared substance abuse outcomes for schizophrenia patients treated with atypical antipsychotic medications versus conventional neuroleptics and tested the interaction of compliance by medication.

Methods: N=404 adult schizophrenia patients were randomly selected from public-sector mental health service systems and enrolled in a 3-year observational study. *Medication type* was coded as: (1) atypical antipsychotic -- including clozapine, risperidone, olanzapine, quetiapine, ziprasidone, or aripiprazole; and (2) conventional neuroleptic -- any other antipsychotic medication. *Substance abuse* was assessed using the adapted MAST (Selzer, 1971) and DAST (Skinner, 1982). Assessments took place every 6-months (N=1832 person-period observations after attrition). Substance abuse was modeled as a function of medication controlling for time, compliance, and relevant covariates using general linear regression for repeated measures (Stokes, Davis, & Koch, 1995).

Results: Baseline prevalence of substance abuse symptoms was 24%; prevalence at the end of the study among retained participants was 16%. Substance abuse was significantly lower for patients treated with atypical antipsychotic medications compared to those treated with conventional neuroleptics (OR = 0.46, $p<0.001$). A significant main effect was found for medication compliance on diminished substance abuse (OR = 0.34, $p<0.001$). Among patients treated with conventional neuroleptics, substance abuse ranged from 31.7% (medication noncompliant) to 22.0% (medication-compliant). Among patients treated with atypical antipsychotics, substance abuse ranged from 16.9% (medication noncompliant) to 6.1% (medication-compliant).

Conclusions: Treatment with atypical antipsychotic medications was associated with significantly lower risk of substance abuse compared to treatment with conventional neuroleptics. Medication compliance also had a significant independent effect in reducing substance abuse. Results seem to indicate an advantage for the atypicals specifically in the treatment of dual disorders. However, their widespread use is tempered by their higher cost. The major limitation of the study is lack of random assignment to treatment group; however, models were adjusted for predictors of medication type.

References:

1. Selzer, ML: The Michigan Alcoholism Screening Test: the quest for a new diagnostic instrument. Am J Psychiatry 1971; 127: 1653-1658.

2. Skinner, HA: The Drug Abuse Screening Test. Addictive Behaviors 1982; 7: 363-371.

NR438 Tuesday, May 23, 12:00 PM - 2:00 PM

A Tale of Two Cities: Lessons Learned From Research Protocol Variance

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Educational Objectives:

Learning Objectives:

1. Compare and contrast the Transition into Primary care Psychiatry-Research Demonstration Project at Thunder Bay and London sites re. protocol variance
2. Lessons learned with respect to barriers encountered in applying a multi-site research project
3. How different interpretations of a model can be implemented

Summary:

Historically models of collaboration have been based on certain fundamental principles such as common purpose, open communication, paradigm, and location of service, business management and relationships. While relationships remain central to the concept of the model, sharing of care among different disciplines is the core element that promotes optimum treatment to improve patient care and satisfaction with the service.

However, much needs to be learned about how a single research protocol could drift and its potential impact on site service delivery. Clinical experience suggests remaining open to new ideas and documenting variations in interpretation is vital so that core components of the collaborative care are continuously respected. Divergent paradigm shifts in a common research model were successfully implemented because the fundamental principles were followed.

Here we report the experience of two sites located in northern and southern Ontario on the successful implementation of a collaborative care approach with some intriguing differences in delivery within the model.

References:

1. Models of Collaboration: A Guide for Mental Health Professionals Working with Health Care Practitioners. David B. Seaburn, Alan D Lorenz, William B Gunn, Jr., Barbara A Gawinski, Larry B Mauksch, New York, Basic Books 1996.
2. Shared Mental Health Care: A Bibliography and Overview. Can J Psychiatry 2002 (APR) (Suppl): 47(2).

NR439 Tuesday, May 23, 12:00 PM - 2:00 PM

Intramuscular Pharmacotherapy of Agitation in Schizophrenia and Bipolar Disorders in Psychiatric Settings at Duke University Medical Center

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Educational Objectives:

Intramuscular use of Typical, Atypical Antipsychotics and Lorazepam with and without Benztropine in agitation in Schizophrenia and Bipolar Disorders.

Summary:

Objective: The availability of newer parenteral psychotropics has expanded the clinicians' armamentarium to treat agitation. However, there are limited data regarding the clinicians' patterns of use of parenteral medications. The aim of this study was to better understand clinicians' preferences regarding the use of Intramuscular (IM) conventional antipsychotics (haloperidol) versus atypical antipsychotics (ziprasidone, olanzapine) with or without lorazepam in the treatment of agitation occurring in schizophrenia and bipolar disorder. *Method*: Clinicians' use of IM Antipsychotics and IM Lorazepam in the Emergency Department and Psychiatric Inpatient unit at DUMC were analyzed using The Clinical Research Information System (CRIS). CRIS is an Electronic Psychiatric Medical Record Repository tool used at DUMC for all clinical and research activities. It has registered 25632 patients and 119086 visits as of September, 2005. This data was analysed from May, 1999 to August, 2005 by looking at total visits, settings (ED and Inpatient), diagnoses (Schizophrenia and Bipolar), Intramuscular administration of older versus newer antipsychotics and Lorazepam.

Results: The rate of usage of IM medications in schizophrenia (SCZ) versus bipolar disorder (BD) is as follows: IM Typical only (SCZ=0.44% versus BD=0.15%), IM Atypical only (SCZ=0.08% versus BD=1%), IM Typical plus Lorazepam (SCZ=0.99% versus BD=1.6%), IM Typical plus Benztropine (SCZ=1.05% versus BD=0.45%), IM Typical/Lorazepam/Benztropine (SCZ=1.4% versus BD=0.40%). None of these differences were statistically significant.

Conclusions: Contrary to most clinicians' perception, the overall usage of intramuscular antipsychotics with or without BDZ was very low in a tertiary Academic Medical center.

References:

1. Zimbroff DL, Allen MH, Battalgia J: Best Clinical practice with Ziprasidone IM CNS Spectr 2005; 10:1-15.
2. Battaglia J: Pharmacological management of acute agitation. Drugs 2005; 65:1207-1222.

NR440 Tuesday, May 23, 12:00 PM - 2:00 PM

Awareness of Cognitive Dysfunction in Patients With Schizophrenia

Alice Medalia, Ph.D. *Bronx, NY*, Julie Thysen, M.A.

Educational Objectives:

At the conclusion of this presentation, the participant should be :

1. familiar with a new instrument that assesses insight into cognitive dysfunction in schizophrenia, and
2. knowledgable about degree of insight that patients with schizophrenia have about their cognitive problems

Summary:

Cognitive functioning is typically impaired in schizophrenia, with the most pronounced deficits in attention, memory and problem solving. Because these cognitive deficits have been linked to poor functional outcome, there is considerable interest in developing treatments for cognitive impairments. Since awareness of need for treatment is predictive of compliance with treatment and better outcome, it becomes important to understand whether people with schizophrenia have awareness of their cognitive deficits. While it is known that insight into psychotic symptoms is typically impaired in schizophrenia, it is not known whether insight into cognitive impairment is similarly impaired. Using a newly developed scale, the Measure of Insight into Cognition (MIC), which measures insight into the cognitive symptoms associated with schizophrenia, we assessed whether impaired insight extends to cognitive symptoms in patients with schizophrenia. We found that self report of awareness of cognitive impairment correlated highly with a clini-

cian report of patient awareness of cognitive impairment, however neither reports of cognitive impairment agreed with the BACS neuropsychological rating of impairment. Patients classified as cognitively impaired with the BACS did not perceive cognitive impairment, suggesting poor awareness of cognitive deficit. Implications for treatment are discussed.

References:

1. Amador XA, Strauss DH, Yale SA, Flaum M M, Endicott J, Gorman J M: Assessment of insight in psychosis. Am J Psychiatry 1993; 15: 873-879.
2. Medalia A & Lim R: Self-awareness of cognitive functioning in schizophrenia. Schizophrenia research 2004; 71: 331-338.

NR441 Tuesday, May 23, 12:00 PM - 2:00 PM

A Six-Week Placebo-Controlled Study on the Safety and Tolerability of Flexible Doses of Oral Paliperidone Extended-Release Tablets in the Treatment of Schizophrenia in Elderly Patients

Andreas Tzimos *Psychiatric Hospital of Thessaloniki, 2nd psychogeriatric ward, 196 LAGADA STR., THESSALONIKI, 56429, Greece*, Michelle Kramer, M.D., Lisa Ford, M.D., Cristiana Gassmann-Mayer, Ph.D., Pilar Lim, Ph.D., Marielle Eerdekens, M.D.

Educational Objectives:

At the conclusion of this presentation, participants should be able to describe the safety and tolerability profile of investigational psychotropic paliperidone extended-release tablets during the treatment of schizophrenia in the elderly.

Summary:

Objective: This study evaluated the safety and tolerability of investigational paliperidone extended-release (paliperidone Extended Release) tablets in elderly schizophrenia patients.

Methods: In this 6-week, double-blind, placebo-controlled study, patients (age ≥65 years) randomly received 6mg/day paliperidone Extended Release (n=76; with flexible doses of 3-12mg/day, 3mg dose increments from Day 7) or placebo (n=38).

Results: Mean age=70 years and modal paliperidone Extended Release dose=6mg/day. Study completion rates were 84% and 68% for paliperidone Extended Release and placebo, respectively, while treatment discontinuations due to adverse events (AEs) were 7% and 8%, respectively. The treatment-emergent AE incidence was comparable for paliperidone Extended Release (67%) versus placebo (71%). The incidence of extrapyramidal disorder was 5% for paliperidone Extended Release compared with 11% for placebo, although hypertonia and tremor occurred only with paliperidone Extended Release (3% each). Serious AEs were reported in the paliperidone Extended Release (3%) and placebo (8%) groups and two patients died in the placebo group. No prolactin or glucose treatment-related AEs or significant changes in mean bodyweight were observed. Mean change (±SD) in PANSS total score at endpoint was -14.6±14.6 (paliperidone Extended Release) and 9.9±15.0 (placebo) (LSM difference -5.5, 95% CI -9.85 to -1.12).

Conclusion: In this study, paliperidone Extended Release (3-12mg/day) was well tolerated and effective in elderly patients with schizophrenia.

References:

1. Alexopoulos GS, Streim J, Carpenter D, Docherty JP; Expert Consensus Panel for Using Antipsychotic Drugs in Older Patients: Using antipsychotic agents in older patients. J Clin Psychiatry 2004; 65(Suppl 2):5-99.
2. Practice guidelines for the treatment of patients with schizophrenia (2nd Edition), February 2004. Available at: http://www.psych.org/psych_pract/treatg/pg/Practice20Guidelines8904/Schizophrenia_2e.pdf.

NR442 Tuesday, May 23, 12:00 PM - 2:00 PM

Association between the DRD3 gene polymorphism (Ser9Gly) and schizophrenia

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to demonstrate clinical implications.

Summary:

Rationale: It is well documented that schizophrenia is associated with dopaminergic dysregulation. Dopaminergic D3 receptors (DRD3), concentrated in limbic-associated structures, may be more particularly involved in schizophrenia. A recent meta-analysis also suggests positive association between the DRD3 Ser9Gly polymorphism and schizophrenia (Psychiatry Genet 2003; 13: 1-12). In the present study, we tried to replicate that finding in a Japanese case-control sample. *Material and Methods*: Our sample includes 246 patients with schizophrenia (DSM-IV) and 198 normal controls. Informed consent was a premise for participation, and this study was approved by the Ethics Committee of the University of Occupational and Environmental Health. Genomic DNA was extracted from 10-ml aliquots of EDTA-anticoagulated venous blood following the standard procedures. Genotyping was assessed by the TaqMan allele-specific assay method using ABI PRISM® 7000 (Applied Biosystems) at the Bio-information Research Center, University of Occupational and Environmental Health. Differences in allele and genotype distribution between cases and controls were evaluated using the χ^2 test. *Results*: Significant association between the DRD3 Ser9Gly polymorphism and schizophrenia was found (genotype: $\chi^2 = 9.76$, df = 2, $p = 0.008$; allele: $\chi^2 = 7.96$, df = 1, $p = 0.0048$; OR = 1.54; 95%CI = 1.14-2.08). *Conclusion*: Our results suggest that it is likely that the DRD3 Ser9Gly polymorphism is associated with schizophrenia in our sample.

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References:

1. Psychiatric Genet, 13, 1-12, 2003.
2. Psychiatric Genet, 13, 1-12, 2003.

NR443 Tuesday, May 23, 12:00 PM - 2:00 PM

Association Between Changes in Negative Symptoms and Functional Outcome Measures in a Stable Schizophrenic Population

Dawn I. Velligan, Ph.D. *University of Texas H.S.C., 7703 Floyd Curl Drive, San Antonio, TX, 78229-3900*, Mai Wang, M.S., George Haig, Pharm.D., Scott Lancaster, M.S., Thomas N. Taylor, Ph.D., Larry Alphs, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to:

1. Demonstrate familiarity with several standard measures of functional outcome in patients with schizophrenia.
2. Describe the degree of correlation between changes in several measures of outcome and scores on the Negative Symptom Assessment Scale.

Summary:

Background: Nearly 1 in 3 patients with schizophrenia have predominant and persistent negative symptoms. The impact of successful treatment of negative symptoms on changes in functionality is not known. This analysis correlated changes in negative symptoms, assessed by Negative Symptom Assessment-16 (NSA-16) scores, with changes in various functional outcome scales. The NSA-16 is a valid and reliable measure of negative symptoms with good rater training efficiency.

Methods: 136 stable outpatients with schizophrenia or schizoaffective disorder participating in 1 of 3 medication or psychosocial treatment intervention studies were assessed at baseline and 3 months on the NSA-16, the Brief Psychiatric Rating Scale (BPRS), the Quality of Life Scale (QLS), the Multnomah Community Ability Scale (MCAS), the Global Assessment of Functioning (GAF), the Social and Occupational Functioning Assessment Scale (SOFAS), the Frontal Systems Behavioral Scale (FrSBe), the Functional Needs Assessment (FNA), and the Life Skills Profile (LSP). The association between change scores (calculated as the difference between scores at baseline and 3 months) was assessed using Pearson's correlation coefficients.

Results: Changes in negative symptoms had moderate to strong statistically significant correlations with changes in functional outcomes. The association was significant for all measures, including structured assessments (QLS, r = -0.423, $P < 0.0001$; MCAS, r = -0.338, P = 0.0008), global assessments (GAF, r = -0.521, $P < 0.0001$; SOFAS, r = -0.497, $P < 0.0001$), and performance-based assessments (FrSBe, r = 0.414, P = 0.0003; FNA, r = -0.231, P = 0.0247; LSP, r = -0.367, P = 0.0003).

Conclusions: Improvements in negative symptoms, as rated by the NSA-16, are associated with improvements in clinician- and patient-assessed functional outcomes measures. This association is particularly strong for the QLS, GAF, and SOFAS. Treatments that improve negative symptoms may reduce the considerable functional disability associated with schizophrenia.

References:

1. Eckert SL, Diamond PM, Miller AL, Velligan DI, Funderburg LG, True JE: A comparison of instrument sensitivity to negative symptom change. Psychiatry Res 1996; 63:67-75.
2. Axelrod BN, Goldman RS, Alphs LD: Validation of the 16-item Negative Symptom Assessment. J Psychiatr Res 1993; 27:253-258.

NR444 Tuesday, May 23, 12:00 PM - 2:00 PM

Ziprasidone in the Treatment of Schizophrenia: Evidence for a Linear Dose-Response Relationship

Lewis E. Warrington, M.D. *Pfizer Incorporated, US Medical, 235 East 42nd Street, 235/10/14, New York, NY, 10017-5755,* Antony D. Loebel, M.D., Ruoyong Yang, Ph.D.

Educational Objectives:

These data will clarify current understanding of the dose-response relationship for ziprasidone in the treatment of schizophrenia.

Summary:

Objective: To clarify the presence of a dose-response relationship for ziprasidone in patients with acute schizophrenia.

Methods: Dose-response analyses were conducted on baseline to end point changes (LOCF) in PANSS total and subscale scores from two similarly designed short-term, placebo-controlled studies using fixed doses of ziprasidone (40 mg/d, n=86; 80 mg/d, n=104; 120 mg/d, n=76; 160 mg/d, n=103; placebo, n=171).

Results: A linear dose-response relationship was detected for change in PANSS total score (F = 12.32, P<0.001) and for several PANSS subscales. This was reflected in the larger treatment effect size observed for PANSS total score in the 160 mg/day group versus the 40 mg/day group (0.52 versus 0.31). Larger effect sizes were also found in the 160 mg/day versus the 40 mg/day group for PANSS negative (0.47 versus 0.22) and cognitive cluster improvement (0.59 versus 0.24).

Conclusions: Prior ziprasidone analyses have suggested a strong trend to dose-response. This post-hoc analysis confirms a linear dose-response in two acute schizophrenia studies where the PANSS was obtained.

Support for this study was provided by Pfizer, Inc.

References:

1. Keck P Jr, Buffenstein A, Ferguson J, et al. Ziprasidone 40 and 120 mg/day in the acute exacerbation of schizophrenia and schizoaffective disorder: a 4-week placebo-controlled trial. Psychopharmacology (Berl) 1998;140:173-184.
2. Daniel DG, Zimbroff DL, Potkin SG, et al. Ziprasidone 80 mg/day and 160 mg/day in the acute exacerbation of schizophrenia and schizoaffective disorder: a 6-week placebo-controlled trial. Ziprasidone Study Group. Neuropsychopharmacology 1999;20:491.

NR445 Tuesday, May 23, 12:00 PM - 2:00 PM

Early Onset of Antipsychotic Action in the Treatment of Acutely Agitated Patients With Schizophrenia

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Educational Objectives:

These research data will contribute to the participant's understanding of the rapid onset of antipsychotic action in patients with acute agitation.

Summary:

Objective: We tested the hypothesis that a rapid onset of antipsychotic effect can occur within the first 24 hours of IM ziprasidone treatment.

Methods: In a 24-hour, double-blind study, hospitalized schizophrenic patients with acute agitation were randomized to treatment with fixed doses of 2 mg IM ziprasidone (N=38) or 20 mg IM ziprasidone (N=41). Efficacy evaluation was based on PANSS, CGI-S, and Behavioral Activity Rating (BARS) scales at 4 and 24 hours. Improvement in psychosis was evaluated by the PANSS positive subscale and an additional psychosis factor (conceptual disorganization, hallucinatory behavior, and unusual thought content) used in previous research[1].

Results: Ziprasidone IM 20 mg produced significantly greater improvement on both the PANSS positive (p=0.032) and psychosis (p=0.038) factors at 24 hours compared to the 2 mg group, in addition to significant improvement in PANSS total (p=0.03). Significant improvement in other components of psychopathology, including CGI-S, CGI-I, PANSS anxiety, and excitement subscales, was first observed at 4 hours and maintained at 24 hours.

Conclusion: Our findings suggest that, in addition to the reduction in acute agitation, IM atypical agents may be associated with a more rapid improvement in psychotic symptoms than has been previously reported.

Support for this study was provided by Pfizer, Inc.

References:

1. Kapur S et al. Evidence for onset of antipsychotic effects within the first 24 hours of treatment. Am J Psychiatry 2005; 162:1-8.
2. Daniel D et al. Intramuscular (IM) ziprasidone 20 mg is effective in reducing acute agitation associated with psychosis: a dou-

ble-blind, randomized trial. Psychopharmacology 2000; 155: 128-124.

NR446 Tuesday, May 23, 12:00 PM - 2:00 PM

A Pooled Analysis of Metabolic Risk Factors for Diabetes Mellitus in Patients Receiving Aripiprazole for Psychotic and Nonpsychotic Disorders

Peter Weiden, M.D. *SUNY Health Science Center at Brooklyn, 450 Clarkson Avenue, Box 1203, Brooklyn, NY, 11203*, Berit Carlson, Ph.D., Stephen Kaplita, M.S., Philippe Auby, M.D., Frederick Grossman, D.O., Richard Whitehead, Ph.D., Christopher Breder, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to appreciate that increased body weight and detrimental changes in lipid levels can occur with the use of certain antipsychotic medications. They should also be able to appreciate that aripiprazole is generally weight neutral and may have positive effects on lipid levels, as demonstrated by a pooled analysis of 13 placebo-controlled trials for schizophrenia, bipolar disorder, and psychosis associated with Alzheimer's disease.

Summary:

Objective: Assess treatment-emergent changes in diabetes-predisposing risk factors (body weight and lipid changes) in safety populations from 13 randomized double-blind, placebo-controlled trials of aripiprazole (2-30mg/d) for schizophrenia (four 4-week, one 6-week, one 26-week), bipolar mania (five 3-week), or psychosis associated with Alzheimer's disease (two 10-week).

Methods: Patient numbers for each assessed variable were governed by laboratory tests performed during each trial. Data for body weight (stratified by baseline Body Mass Index [BMI]) were pooled from all trials except 2 of the bipolar studies. Data for fasting total cholesterol (aripiprazole=474, placebo=314) were pooled from the 6- and 26-week schizophrenia trials, 5 bipolar trials, and the 2 Alzheimer's disease trials. Fasting patient data for triglycerides (aripiprazole=212, placebo=125), low-density lipoproteins (LDL: aripiprazole=205, placebo=123), and high-density lipoproteins (HDL: aripiprazole=211, placebo=124) were pooled from the 6- and 26-week schizophrenia trials. Mean changes (baseline to endpoint) were analyzed using ANCOVA.

Results: Across all trials, aripiprazole was associated with a minimal mean body weight increase of 0.2±0.1kg (placebo, -0.1±1.1kg; P=0.024). For BMI <23, body weight increased ≥7% in 13.1% of aripiprazole-treated patients (n=388) versus 5.9% of placebo-treated patients (n=254; P<0.05). For BMI 23-27, percentage of patients with body weight increases ≥7% was similar between aripiprazole-treated (5.9%, n=392) and placebo-treated patients (4.7%, n=235; P=0.88). For BMI >27, body weight increased ≥7% in 2.7% of aripiprazole-treated patients (n=699) versus 1.0% of placebo-treated patients (n=388; P≤0.05). There were no significant differences between aripiprazole-treated and placebo-treated patients in fasting cholesterol, triglyceride, or LDL concentrations. Mean change in fasting HDL concentration slightly favored aripiprazole versus placebo (difference=2.5mg/dL; P<0.05).

Conclusion: Multiple randomized, double-blind, placebo-controlled trials indicate that aripiprazole is generally weight neutral and does not negatively affect lipid profiles.

References:

1. Marder SR, McQuade RD, Stock E, et al: Aripiprazole in the treatment of schizophrenia: safety and tolerability in short-term, placebo-controlled trials. Schizophr Res 2003; 61:123-136.
2. McQuade RD, Stock E, Marcus R, et al: A comparison of weight change during treatment with olanzapine or aripiprazole: results from a randomized, double-blind study. J Clin Psychiatry 2004; 65(Suppl 18):48-56.

NR447 Tuesday, May 23, 12:00 PM - 2:00 PM

Use of Long-Acting Antipsychotic Injection Medications for Medication Non-Adherence in Schizophrenia

Joyce C. West, Ph.D. *APIRE, Practice Research Network, 1000 Wilson Boulevard, Arlington, VA, 22209*, Joshua E. Wilk, Ph.D., Steven Marcus, Ph.D., Lisa M. Countis, Darrel A. Regier, M.D., Mark Olfson, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to: 1) understand patient and psychiatrist factors associated with initiation of long-acting intectable antipsychotic medications; and 2) identify clinical, setting and clinician determinants associated with potential under-utilization of long-acting injectable antipsychotic medications.

Summary:

ABSTRACT

Objective: Describe patient and psychiatrist characteristics associated with initiation of long-acting antipsychotic injections in a nationally representative sample of psychiatric outpatients with schizophrenia and recent medication non-adherence.

Methods: A national survey was conducted among a random sample of psychiatrists treating schizophrenia. Each psychiatrist reported on one adult outpatient with schizophrenia who was non-adherent with oral medications at some point in the last year. 69% of eligible psychiatrists responded, resulting in a sample of 295 patients. Rates of initiating long-acting injections are compared across patient and psychiatrist characteristics.

Results: 17.6% of patients initiated long-acting antipsychotic injections. In regressions controlling for relevant patient and psychiatrist characteristics, initiating long-acting injections was significantly and positively associated with: public health insurance (OR= 19.0; 95% CI 2.3-160.4); inpatient admission during the episode of non-adherence (OR=3.3; 95% CI 1.6-7.1); medication non-adherence for a greater proportion of time under treatment (OR= 2.6; 95% CI 1.1-5.9); average or above average intellectual functioning (OR=2.8; 95% CI 1.1-7.4); and living in a mental health residence (OR=4.1; 95% CI 1.4-12.3). Use was inversely associated with using second generation antipsychotics (OR=.23; 95% CI .1-.6) and other oral psychotropic medications prior to medication non-adherence (OR=.3; 95% CI=.1-.8). Psychiatrists who were male (OR=3.0; 95% CI 1.2-7.7), nonwhite (OR=2.1 (95% CI 1.1-4.3), and more optimistic about management of non-adherence (OR=6.1; 95% CI 2.3-16.6) were more likely to initiate long-acting injections.

Conclusions: Despite clinical recommendations urging use of long-acting preparations for schizophrenia patients with medication non-adherence, they are uncommonly used in practice. Initiation of long acting antipsychotic injections appears to be a joint function of patient, physician, treatment, and setting related factors.

References:

1. Citrome L, Levine J, Allingham B: Utilization of depot neuroleptic medications in psyciatriatric inpatients. Schiz Bull 1996;32:321-326.
2. Keith SJ, Pani L, Nick B, Emsley R, San L, Turner M, Conley R, Scully P, CHue PS, Lachaux B: Practical application of pharmacotherapy with long-acting risperidone for patients with schizophrenia. Psych Serv 2004;55:997-1005.

NR448 Tuesday, May 23, 12:00 PM - 2:00 PM

Family Contact and Management of Medication Non-adherence in Schizophrenia

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to identify the interventions most commonly used by psychiatrists in the management of medication non-adherence among patients with schizophrenia with high versus low levels of family contact.

Summary:

Objectives: Compare and contrast: 1) specific types of interventions to address medication non-adherence among patients with schizophrenia with high (daily contact with family or live with spouse or parents) versus low levels of family contact; and 2) perceived effectiveness of medication non-adherence interventions among patients with schizophrenia with high versus low levels of family contact. **Methods:** A national survey was conducted among a random sample of psychiatrists treating schizophrenia. Each psychiatrist reported on one adult outpatient with schizophrenia who was non-adherent with oral medications at some point in the last year. 69% of eligible psychiatrists responded, resulting in a sample of 295 patients. Patients with high versus low levels of family contact were compared. **Results:** Psychiatrists used a family intervention with 67% of the sample. Psychiatrists were more likely to use family interventions to manage medication non-adherence among patients with high family contact, such as teaching the family about the patient's illness and treatment ($p<.01$), and exploring the family's attitudes toward medication ($p<.01$). Although depot medications were reported to be among the most effective interventions for both groups, they were less likely to be used with the high family contact group ($p=.05$). There were generally few differences between patient groups in psychiatrists' perceived effectiveness of psychopharmacological, psychological, and behavioral interventions; however, observed differences were in the direction of greater effectiveness in patients with high family contact. Family interventions generally were rated significantly more effective with patients with high family contact ($p<.01$). **Conclusion:** Although previous research suggests family interventions are used with a minority of families, these findings found that psychiatrists reported using family interventions with most patients. Several interventions were reported significantly more effective in the high family contact group, reinforcing the potential benefit of family support in managing antipsychotic non-adherence.

References:

1. Dixon L: Providing services to families of persons with schizophrenia: Present and future. J Ment Health Policy Econ 1999; 2: 3-8.

2. Razali MS, Yahya H: Compliance with treatment in schizophrenia: A drug intervention program in a developing country. Acta Psychiatr Scand 1995; 91: 331-335.

NR449 Tuesday, May 23, 12:00 PM - 2:00 PM

Individual Sleep Quality and Neighborhood Perceived Security: A Multilevel Analysis

Chien-Chang Wu, M.D. *Taipei City Psychiatric Center, 309 Songde Road, Taipei, 110, Taiwan Republic of China*, Ying-Yeh Chen, Sc.D., Ichiro Kawachi, Ph.D., S. V. Subramanian, Ph.D.

Educational Objectives:

1. At the conclusion of this presentation, the participant should be able to recognize that both individual and contextual factors determine individual sleep quality.
2. One of the important strengths of multilevel analysis lies in its ability to disentangle the contextual and individual source of variation in individual sleep quality. That is, controlled for individual characteristics, multilevel analysis can estimate the independent effects of contextual factors on individual sleep quality. In addition, differential effects of the context on different groups of people can be examined.
3. Perceived security at the neighborhood level, a proxy for neighborhood social capital, is positively associated with individual sleep quality.
4. Policies that enhance neighborhood perceived security can improve individual sleep quality. Integrated research on social, criminal justice, and mental health policies is important for insomnia management.

Summary:

Background: Insomnia is one of the most frequently encountered mental health problems. Environmental factors have been shown to be associated with insomnia; however research on the effects of neighborhood social milieu on individual sleep quality has been scarce.

Objective: This study examines whether perceived security at the neighborhood level predicts individual sleep quality, controlling for individual factors.

Methods: The dataset used is a representative sample from a cross-sectional survey, the Taiwan Social Trends Survey. It comprises four levels: 39,588 individuals at level-1 were nested in 13,605 households at level-3, which were nested in 871 neighborhoods at level-3, and finally in 23 cities and counties at level-4. We conducted a four-level random intercept multilevel analysis to control for clustering effects and to examine contextual and compositional factors in sleep quality. The outcome variable, individual sleep quality, was constructed by aggregating the scores from the Insomnia Self-assessment Inventory. We used the percentage of surveyed people feeling secure in their neighborhoods as the main predictor, neighborhood perceived security.

Results: As neighborhood perceived security increased, individual sleep quality increased in all groups of surveyed people ($p<0.001$). Although violence victims generally slept less well than non-victims, their individual sleep quality were more responsive to increased level of neighborhood perceived security ($p<0.07$). In contrast, disadvantaged groups such as the elderly, the retired/disabled, the unhealthy, the divorced, widowed and separated benefited less from an increase than their relevant comparison groups ($p<0.05$).

Conclusion: Although neighborhood perceived security is beneficial to all groups of people, not all of them enjoy the benefit to the same degree. Good policies to improve mental health, individual sleep quality in particular, should take into account individual characteristics as well as neighborhood social milieu.

References:

1. Chandola T: The fear of crime and area differences in health. Health & Place 2001; 7: 105-116.

2. Diez-Roux AV: The examination of neighborhood effects on health. In Neighborhoods and Health, edited by Kawachi I, Berkman LF, New York, Oxford University Press, 2003, pp45-64.

NR450 Tuesday, May 23, 12:00 PM - 2:00 PM

Mental Retardation and Psychosis Comorbidity: Where Do We Stand in Diagnostic Overshadowing?

Irem Yalug *Kocaeli University Medical Faculty, Gardenya 5/5B Daire:40 Atasehir, Istanbul, Turkey*, Ali Evren Tufan, Eylem Ozten

Educational Objectives:

At the conclusion of this presentation the participant should be able to recognize mental retardation in differential diagnosis of adult psychopathology.

Summary:

Objective: Psychiatric problems in mild mental retardation (MR) are similar but more frequent to general population but, they change in frequency and presentation in severely retarded. The objective of this study is to evaluate the prevalence of psychopathology and characteristics of mentally retarded patients treated on an inpatient basis in a tertiary treatment center during a five year period.

Methods: Records of patients hospitalised for treatment in Kocaeli University Medical Faculty Department of Psychiatry between 2000 and 2005 were reviewed retrospectively and patients with MR or borderline intellectual functioning were identified. Sociodemographic and clinical variables were recorded and analysed with SPSS 10.0 program via descriptive statistics. Chi square test was used to determine the relation between length of hospital stay and sociodemographic and clinical variables. P was set at 0.05

Results: The prevalence of MR was found to be 4% for a five year period. 94 % of the patients had mild MR. Mean age of the patients was 28 (SD 10.8) years. Mean duration of inpatient treatment was 30.7 (SD 78.9) days. 70% of the patients were female and 60 % did not comply with treatment. The commonest axis I diagnosis was psychosis with a prevalence of 40 %. The prevalence of schizophrenia was found to be 25 %. Only in 20% of patients MR was identified before hospitalisation. 35 % of patients attempted suicide.

Length of hospitalisation tended to be affected by the number of suicide attempts (p=0.06) and type of antipsychotics used (p= 0.09). Patients using typical antipsychotics tended to stay for shorter periods.

Discussion: The lack of identification of MR before hospitalisation in our sample was striking. MR should be part of differential diagnosis in adult psychopathology. Suicide history should be taken in MR patients. Shorter hosptalisation with typical antipsychotics may be due to sedation.

References:

1. Lund J. The presence of psychiatric co-morbidity in mentally retarded adults. Acta Psychiatr Scand 1985; 72: 563-570.
2. Cooper SA. Epidemiology of psychiatric disorders in elderly compared with younger adults with learning disabilities. Br J Psychiatry 1997; 170: 375-380.

NR451 Tuesday, May 23, 12:00 PM - 2:00 PM

Diagnostic Stability of Patients With Schizophrenia: An Investigation Based on National Health Insurance Database in Taiwan

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Educational Objectives:

The participants should learn that taking Taiwan's national insurance database as an example, the diagnostic stability of schizophrenia was similar compared to other countries. Age, diagnoses made by the same psychiatrist, diagnosis made by the same hospital, and hospital type of final diagnosis were associated with the diagnostic stability of schizophrenia while gender and time interval between diagnoses were not.

Summary:

Objective: To investigate factors associated with change in diagnosis from schizophrenia to other disorders and from others to schizophrenia.

Methods: This nationwide investigation was based on claim database from the National Health Insurance (NHI) of Taiwan. The data comprised of population who had inpatient record to psychiatric section from 1995 to 2001 and were followed up to the end of 2003. The inclusion criteria are at least one inpatient record with schizophrenic diagnosis and re-admission records from 1997 to 2001. Those schizophrenic patients who had inpatient record in 1995 and 1996 were excluded. The study population was divided into 4 non-overlapping groups: 1. stable schizophrenia, 2. change from schizophrenia to others, 3. from others to schizophrenia, and 4. from another to schizophrenia then others. The associated factors were investigated by the one-way ANOVA, chi-square test and generalized logits model.

Results: The subjects were 13337 inpatients with male predominant (58.6%), had admission for averaged 4.3+3.3 times, and first admission record at the age of 34.3 (SD=13. 8). 84.5% (8285/9806) of the patients first diagnosis of schizophrenia remained the same diagnosis of schizophrenia to the end of observation. 1521 subjects change to others, 1981 patients change from others to schizophrenia and 1550 change from others to schizophrenia then another. In the final statistic model, age between 20 and 60 years old, diagnoses made by the same psychiatrist, diagnosis made by the same hospital and final diagnosis at psychiatric hospital (compared to general hospital) were associated with the diagnostic stability of schizophrenia ($p<.0001$) while gender, hospital type of initial diagnosis, and time interval between diagnoses were not.

Conclusions: The positive predictive rate of schizophrenia diagnosis was similar worldwide. Whether the diagnosis change was due to changes in the clinical state of the patients or other factors needs a longitudinal follow-up study to answer.

References:

1. Chen Y, Swann AC, Burt DB: Stability of diagnosis in schizophrenia. Am Journal Psychiatry 1996;140: 682-6.
2. Munk-Jorgensen P: The schizophrenia diagnosis in Denmark. A register-based investigation. Acta Psychiatrica Scandinavica 1985;72: 266-73.

NR452 Tuesday, May 23, 12:00 PM - 2:00 PM

Dimensions of Psychosis in Patients With Bipolar Mania

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to identify similar clusters of psychotic symptoms in patients with bipolar disorder and schizophrenia.

Summary:

Background: Psychosis is present in approximately 50% of patients with bipolar mania and is commonly evaluated in clinical research and trials by means of the PANSS. A factor analysis of the baseline PANSS scores in patients with bipolar mania was

conducted to identify factors or dimensions of the psychosis in these patients.

Methods. Data were analyzed from two 3-week, double-blind, placebo-controlled studies of risperidone monotherapy for acute manic or mixed episodes associated with bipolar I disorder (N= 546). Patient inclusion criteria included a DSM-IV diagnosis of bipolar I disorder with manic or mixed episode, with or without psychotic features, age ≥ 18 years, and mean baseline Young Mania Rating Scale (YMRS) scores ≥ 20. A principal component analysis of the 30 PANSS item scores of these patients at baseline was conducted. To examine the sensitivity of the analysis, 5 additional factor analyses were performed on 85% of randomly selected subjects from the total sample of 546.

Results: Five factors were extracted by the analysis: anxiety/depression, negative/cognitive, excitement, positive symptoms, and negative symptoms. A prior factor analysis of PANSS data in patients with schizophrenia spectrum disorders (N=2579) or bipolar I disorder (N=505) by Lindenmayer et al (Schizophr Res, 2004) also extracted 5 factors in both the schizophrenia and bipolar patients: negative symptoms, positive symptoms, cognition, excitement, and depression/anxiety. Five similar factors in patients with schizophrenia were also identified by Marder et al (J Clin Psychiatry, 1997). Conclusion: The results of the present analysis and those of other studies indicate similarities in psychotic symptom factors in patients with bipolar mania and schizophrenia. Future analyses of the present study will address the effects of treatment on the identified factors. Supported by Janssen, L.P.

References:

1. Lindenmayer J-P, Brown E, Baker RW, et al. An excitement factor of the Positive and Negative Syndrome Scale. Schizophr Res 2004;68:331-337.
2. Marder SR, Davis JM, Chouinard G. The effects of risperidone on the five dimensions of schizophrenia derived by factor analysis: combined results of the North American trials. J Clin Psychiatry 1997;58:538-546.

NR453 Tuesday, May 23, 12:00 PM - 2:00 PM

Augmentation of Clozapine With Amisulpride in Patients With Treatment-Resistant Schizophrenia: An Open Clinical Study

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that in patients with treatment resistant schizophrenia augmentation strategies are one possible treatment option.

Summary:

Background: Therapeutic options for patients with treatment-resistant schizophrenia are limited. In such cases combined application of atypical antipsychotic drugs is an often used strategy. We tested the hypothesis that the combination of amisulpride and clozapine would lead to an long term improvement in these patient group.

Objectives: 15 patients with treatment-resistant schizophrenia participated in this open clinical trial and recieved a combination of amisulpride and clozapine. Patients had to have remained on a stable dose of clozapine for at least 6 months in order to ensure a reasonable opportunity to respond to clozapine monotherapy. Clinical status was evaluated at baseline 3, 6 and 12 months follow-up using the Brief Psychiatric Rating Scale (BPRS).

Results: All patients completed 12 months combination treatment. The mental state of 11 patients (73.3%) was improved and there was a significant reduction in the mean BPRS score over the 12 months of combination treatment. The augmentation of amisulpride in clozapine treated patients did not result in a corresponding increase in side effects. The combination allowed a mean reduction of 12.8% of the daily clozapine dose.

Conclusions: The combined application of clozapine and amisulpride follows a neurobiological rationale and appears to be safe and well tolerated without increasing the risk of side effects.

References:

1. Munro J, Matthiasson P, Osborne S et al. Amisulpride augmentation of clozapine: an open non-randomized study in patients with schizophrenia partially responsive to clozapine. Acta Psychiatr Scand 2004; 110:292-298.
2. Lerner V, Bergman J, Borokhov A et al. Augmentation with Amisulpride for schizophrenic patients nonresponsive to antipsychotic monotherapy. Clin Neuropharmacol 2005;28:66-71.

NR454 Tuesday, May 23, 12:00 PM - 2:00 PM

Effectiveness of a Single Intramuscular Injection of Aripiprazole in Patients With Schizophrenia or Bipolar Disorder, Stratified by Levels of Agitation

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to appreciate that patients with schizophrenia or bipolar I disorder each exhibit a spectrum of symptoms, some of which are common to both, such as agitation. They should be aware that symptoms of agitation are significantly reduced within 2 hours of a single intramuscular injection of aripiprazole or haloperidol, as demonstrated by a pooled analysis of efficacy data from two placebo-controlled trials of patients with schizophrenia. They should also be aware that a single intramuscular injection of aripiprazole or lorazepam significantly reduces symptoms of agitation, as demonstrated by an analysis of efficacy data from a trial of patients with bipolar I disorder.

Summary:

Objective: Evaluate the effectiveness of single aripiprazole IM injections to reduce agitation associated with acute schizophrenia or bipolar I disorder.

Methods: Agitation was defined as baseline PANSS Excited Component (PEC) score of 15-32 (median=18). Patients with PEC scores above/below 18 were designated as more/less agitated, respectively. Data were pooled across dosing arms from two studies of patients with schizophrenia (N=739) receiving IM aripiprazole (5, 10, or 15mg), haloperidol (6.5 or 7.5mg), or placebo. Data from one study of patients with bipolar I disorder (N=291) receiving IM aripiprazole (10 or 15mg), lorazepam (2mg), or placebo were pooled across doses and analyzed separately. PEC scores were assessed 2 hours after a single injection to measure efficacy. Mean change from baseline comparisons were analyzed using an ANCOVA model controlling for treatment, protocol, and baseline value.

Results: In the schizophrenia study, the more agitated patients (baseline PEC scores >18) treated with aripiprazole (n=187) or haloperidol (n=111) experienced significant decreases in PEC scores (-8.1 and -9.1, respectively [baseline-to-endpoint]) versus placebo (-4.0; $P<0.01$ [n=65]). In less agitated patients with schizophrenia, aripiprazole (n=162) and haloperidol (n=130) were also associated with significantly reduced PEC scores (-7.1 and -7.0, respectively) versus placebo (-5.6 [n=84]; $P<0.01$ [aripiprazole], $P<0.05$ [haloperidol]). In the bipolar study, the more agitated pa-

tients treated with aripiprazole (n=62) or lorazepam (n=25) experienced decreases in PEC scores (-9.9 and -11.4, respectively [baseline-to-endpoint]) that were not significantly different from placebo (-7.9; n=21). In less agitated patients with bipolar disorder, aripiprazole (n=88) and lorazepam (n=43) were associated with significantly reduced PEC scores (-7.9 and -8.4, respectively) versus placebo (-4.4; $P<0.01$ [n=52]).

Conclusions: IM aripiprazole effectively reduced agitation within 2 hours in patients with schizophrenia or bipolar I disorder.

References:

1. Oren D, Iwamoto T, Marcus R, et al : Intramuscular Aripiprazole vs Placebo for Agitation in Acute Mania. Presented at: Annual Meeting of the American Psychiatric Association, Atlanta, GA, USA, May 21-26, 2005.
2. Yocca F, Marcus M, Oren D, et al: Intramuscular Aripiprazole in Acute Schizophrenia: A Pivotal Phase III Study. Presented at: Annual Meeting of the American Psychiatric Association, Atlanta, GA, USA, May 21-26, 2005.

NR455 Tuesday, May 23, 12:00 PM - 2:00 PM

Comparison of Agitation Reduction Techniques in the Emergency Department

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Educational Objectives:

The purpose of this study was to assess what, if any agitation reduction techniques are used prior to restraints in the Emergency Department as recommended by the JCAHO. The second purpose was to determine the reasons for differing levels of usage and or compliance with the JCAHO recommendations.

Summary:

Introduction: JCAHO and numerous advocacy groups mandate the use of alternatives to restraints. The purpose of this study was to assess what, if any, alternatives are used in the Emergency Department (ED). The second purpose was to determine the reasons for differing levels of usage and or compliance with these recommendations.

Methods: A survey tool was developed and piloted. It was sent to a random sample of 20% of the EDs and to all Psychiatric EDs from AAEP. The survey included questions on the use and effectiveness of alternatives, training in how and when to use those methods, and reasons why they do or do not use them in the ED. The study was IRB approved.

Results: There were 209 of 817 responses at this time. The majority 57% of the ED's have no psychiatric unit. The overwhelming majority at 84% do use alternatives to restraints prior to restraints. When restraints are used 30% used physical and 30% used physical and chemical combined. A management protocol was in place at 63% of the institutions to use alternative first and 76% of the staff is educated on the use of alternative methods. The methods in order of popularity are verbal interventions at 84%, one- on one at 79%, decrease in simulation at 74%, food or during at 69%, The rating of the effectiveness was low with less 48% feeling one on one, 36% verbal intervention, 15% decreasing stimulation and 18% food or drink as being effective. However, 61% felt that pharmaceutical restraints were effective.

Discussion: The majority of respondents have training on alternatives to restraints. They used alternative to restraints with one to one, food or drink and verbal interventions being the most frequently used. They were seen as not being very effective.

References:

1. Zun, LS: Complications of Patient Restraints, J Emerg Med 2003; 24:119-124.
2. Zun, LS: Evidence-based treatment of psychiatric patient.J Emerg Med. 2005;28:277-83.

NR456 Tuesday, May 23, 12:00 PM - 2:00 PM

Pharmacoeconomics: Divalproex Sodium and Schizophrenia Spectrum Disorders

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Educational Objectives:

At the conclusion of this session, the participants should better understand the economic impact of the adjunctive use of divalproex sodium in patients with schizophrenia with schizophrenia spectrum disorders.

Summary:

Objective: Using a retrospective chart review method with the pretreatment period as a comparator, we examined economic impact as reflected in bed days of hospital care of the adjunctive use of divalproex sodium (DIV).

Method: A chart review was conducted on over 350 charts of patients identified from pharmacy records as receiving at least one prescription of DIV. Of these, 48 carried a chart diagnosis of Schizophrenia spectrum disorders, and had satisfactory evaluable pre- and post-initiation epochs (i,e.,one year before and two years after DIV).

Results: Exactly 39.6% schizophrenia 60.4% schizoaffective; 6.3% women 93.8% men. Average dose of DIV was 1452.23 mg/d (SD=695.75). Average days of hospitalization per year increased from 15.38 (SD=28.59) to 31.96 (SD=46.99) avter initiating DIV. This is a statistically significant increase (p=.001). There was no differnce in hospital days between year 1 and year 2 with DIV (p= 0.303), or between the number of patients on antideprressants (p=0.689) and mood stabilizers (p=0.813) before and during treatment of DIV. Cost of hospitalization increased from $12, 800.00/year/patient to $25,600.00

Conclusion: This retrospective chart review analysis suggests that initiation of adjunctive DIV is either a marker for impending clinical instability or of limited therapeutic and negative economic consequences.

Supported by Abbott Pharmaceuticals

References:

1. Moringo A, Martin J, Gonzalez S, Mateo I. Treatment of resistant schizophrenia with valproate and neuroleptic drugs. Hillside K Clin Psychiatry 1989:11:199-207.
2. McElroy SL Keck PE, Pope HG. Sodium valproate: its use in primary psychiatric disorders. J Clin Psychopharmacol 1987;7:16-24.

NR457 Tuesday, May 23, 3:00 PM - 5:00 PM

Efficacy of Tadalafil (Cialis ®) in Anorgasmic Women Taking Selective Serotonin Reuptake Inhibitors (SSRIs)

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to:

1. Recognize and evaluate sexual dysfunction in women induced by Selective Serotonin Reuptake Inhibitors (SSRIs).

2. Use the Sexual Function Index Rating to assess sexual dysfunction and its improvement.

3. Understand the use and limitations of off-label tadalafil (Cialis ®) in reversing sexual dysfunction in women.

Summary:

Objectives: The purpose of this preliminary study was to determine the response of women with SSRI or menopause-induced sexual dysfunction treated before sexual activity with tadalafil at varying dosage levels. METHODS: 10 anorgasmic women, ages 27 to 61, seven using SSRIs or NSRIs and seven menopausal, were entered in this open-label study. The patients received 10mg of tadalafil to start, and were given the option to increase this dosage to 20mg and 40 mg. Efficacy was assessed by giving the patients the Sexual Function Inventory (SFI) created by G. Nurnberg et al. (2000) before they received tadalafil while suffering from sexual dysfunction and after trying tadalafil. The test quantifies the domains of interest, arousal, orgasm, lubrication, and overall sexual satisfaction, while predetermining that the sexual dysfunction was not present prior to SSRI use or menopause. Results: Of the group, 10 participated in the study and were available for follow up. Mean baseline SFI score before therapy was 5.29 ± 0.93. The SFI score improved to 3.39 ± 1.95 at 40mg. The mean overall score improved by 35.9%. The mean scores for interest, arousal, and lubrication improved by 17.5%, 45.0%, and 40.2 % respectively. The mean scores for orgasm and satisfaction improved by 46.7% and 27.8% respectively. Overall, only two patients of ten had a significant (over 60% improvement in the mean SFI score). Side effects included upset stomach, cramping, and lower back pain. Conclusions: The data suggests that tadalafil is well tolerated in anorgasmic women taking SSRIs or NSRIs or going through menopause. Overall sexual function did not improve significantly through the use of tadalafil, although there were changes in all of the categories (interest, arousal, lubrication, orgasm, and satisfaction) for the better.

References:

1. Nurnberg HG, Hensley PL, Gelenberg A, Fava M, Lauriello J, Paine S: Treatment of antidepressant-associated sexual dysfunction with sildenafil. JAMA 2003; 289:1:56-63.
2. Balon R: Sexual function and dysfunction during treatment with psychotropic medications. Clin Psychiatry 2005; 66:11:1488-1489.

NR458 Tuesday, May 23, 3:00 PM - 5:00 PM

Sexual Dysfunction in Patients With Major Depressive Disorder: A Comparison Between Selegiline Transdermal System 6mg/24hr and Placebo Using a Patient-Rated Scale

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Educational Objectives:

At the conclusion of this presentation, participants should be able to:

1. Describe the data from 4 short-term studies that examined the effects of selegiline transdermal system (STS) on sexual functions.

2. Demonstrate an understanding of the data indicating that short-term therapy with STS is not associated with a increase in treatment-related sexual side effects.

Summary:

Introduction: Tolerability of pharmacologic agents is paramount for successful treatment of depressive disorders.[1] Side effects, such as sexual dysfunction, impact quality of life and limit patient adherence to medications.[1,2] Selegiline is a MAO inhibitor that has been developed as a transdermal patch for treatment of major depression. Previous studies have reported a low incidence of sexual side effects with selegiline transdermal system (STS) treatment.[3,4]

Objective: To examine the effects of STS treatment on sexual function across multiple controlled trials using a patient-rated scale (MED-D). The MED-D is a 5-item rating scale developed to evaluate sexual interest, arousal, maintenance of interest, climax, and satisfaction.

Methods: In 4 short-term (6 to 8 weeks), double-blind, placebo-controlled clinical studies, adults 18 years or older with a diagnosis of MDD treated with STS 6mg/24hr or placebo were asked to complete the MED-D scale at baseline and at the last study visit. Each symptom was graded on a scale ranging from 1 (not at all) to 5 (severe). Data from the 4 studies compared sexual dysfunction scores between STS- and placebo-treated patients.

Results: There was an overall improvement in sexual functioning during treatment with STS and placebo. In an integrated analysis, mean reductions in MED-D ratings (ie, improvement) were similar between STS- and placebo-treated patients (-1.8 versus -1.1, respectively). Likewise, in individual studies, mean improvement in sexual function was similar during STS and placebo treatment, indicating that STS was not associated with sexual side effects.

Conclusions: Data from 4 placebo-controlled trials indicate that short-term therapy with STS is not associated with an increase in treatment-related sexual side effects or an increase in sexual dysfunction compared with placebo, as measured by a patient-rated scale. These results corroborate other findings of a low incidence of spontaneously reported sexual side effects during STS treatment.

References:

1. Nemeroff CB: Improving antidepressant adherence. J Clin Psychiatry 2003;64 Suppl 18:25-30.
2. Zimmerman N, Pasternak MA, Attiulah N, Friedman M, Boland RJ, Baymiller S, Berlowitz SL, Rahman S, Uy KK, Singer S, Chelminski I: Why isn't bupropion the most frequently prescribed antidepressent? J Clin Psychiatry 2005;66:603-610.

NR459 Tuesday, May 23, 3:00 PM - 5:00 PM

Early Response to Antipsychotics as Predictor of Later Response in the Naturalistic Treatment of Schizophrenia

Haya Ascher-Svanum *Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN, 46285*, Allen Nyhuis, Douglas E. Faries, Bruce J. Kinon

Educational Objectives:

At the conclusion of this presentation, the participant should recognize that in the naturalistic treatment of patients with schizophrenia, lack of early minimal response to treatment with antipsychotic medications, as measured by the PANSS total score (or 4 psychotic items), appears to accurately predict subsequent non-response to treatment. These findings suggest that early non-responders may benefit from change in antipsychotic regimens to avoid prolonging exposure to sub-optimal treatment alternatives.

Summary:

Objective: To assess whether early response to antipsychotic medication (at 2 weeks) accurately predicts later response (at 8 weeks) in the naturalistic treatment of schizophrenia.

Methods: Data were drawn from a randomized, open-label, trial (N=664) of olanzapine, risperidone, and typical antipsychotics in the treatment of schizophrenia, completed in September 2002.

Treatment response was defined as at least 20% improvement on the PANSS total score from baseline ("minimal improvement"). Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall predictive accuracy were calculated for response/non-response at 2 weeks and subsequent response/non-response at 8 weeks. Analyses were repeated using mild or better scores on 4 PANSS psychotic items to define response.

Results: Early response/non-response predicted subsequent response/non-response with high overall accuracy (72.8%), moderate PPV (69.4%), high NPV (73.8%), moderate sensitivity (42.4%), and high specificity (89.7%). Results were similar when 4 PANSS psychotic items defined response/non-response. **Conclusions:** In the naturalistic treatment of schizophrenia, early response/non-response to treatment with antipsychotics appears to accurately predict subsequent response/non-response to treatment. Findings suggest that early non-responders may benefit from change in antipsychotic regimens to avoid prolonging exposure to sub-optimal treatment alternatives. Findings are consistent with previous research on early prediction of antipsychotic response in schizophrenia.

References:

1. Correll CU, Malhotra AK, Kaushik S. et al. Early prediction of antipsychotic response in schizophrenia. Am J Psychiatry 2003;160:2063-2065.
2. Kapur S, Arenovich T, Agid O et al. Evidence for onset of antipsychotic effects within the first 24 hours of treatment. Am J Psychiatry 2005;162:939-946.

NR460 Tuesday, May 23, 3:00 PM - 5:00 PM

The Three-Year Course of Schizophrenia Among Persons With Tardive Dyskinesia and Persons Without

Haya Ascher-Svanum *Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN, 46285*, Baojin Zhu, Douglas E. Faries, Bruce J. Kinon, Mauricio F. Tohen, Mauricio F. Tohen

Educational Objectives:

At the conclusion of this presentation, the participant should recognize that the course of schizophrenia significantly differs between persons with tardive dyskinesia (TD) and persons without. Persons with TD appear to have a more severe illness profile and more refractory course of illness, suggesting poorer prognosis and the need for specialized targeted interventions.

Summary:

Objective: To compare the 3-year course of schizophrenia between persons with tardive dyskinesia (TD) and persons without.

Methods: Data were drawn from a large, prospective, naturalistic study of persons treated for schizophrenia in the US, conducted between 7/1997 and 9/2003. Treatment outcomes were assessed at 12-month intervals using standard psychiatric measures and medical record abstraction. Using repeated measures analyses, participants with probable TD at enrollment (fulfilling Schooler-Kane criteria, N=621, 29.5%) were compared with participants who did not (N=1482), on clinical and functional measures across the 3-year study.

Results: Participants with TD had, across the 3-year study, significantly more severe psychopathology (PANSS total score, negative symptoms, positive symptoms, general psychopathology), were less likely to experience symptom remission, had more severe EPS, and poorer level of functioning (eg, productivity level, employment, daily activity, GAF, Quality of Life Scale and its 4 domains). Results were essentially unchanged following adjustments for known correlates of TD and when using a subgroup of participants with persistent TD (at enrollment and at 1 year).

Conclusions: In the long-term treatment of schizophrenia, persons with TD have a significantly more severe and more refractory course of illness than persons without TD, suggesting poorer prognosis and need for specialized interventions.

References:

1. Miller DD, McEvoy JP, Davis SM, et al. Clinical correlates of tardive dyskinesia in schizophrenia: Baseline data from the CATIE schizophrenia trial. Schizophr Res. 2005 Sep 17.
2. Browne S, Roe M, Lane A. et al. Quality of life in schizophrenia: relationship to sociodemographic factors, symptomatology and tardive dyskinesia. Acta Psychiatr Scand. 1996 Aug;94(2):118-24.

NR461 Tuesday, May 23, 3:00 PM - 5:00 PM

Studies on the Potential for Pharmacokinetic Drug Interactions Between the Selegiline Transdermal System 6mg/24hr and Three Psychotropic Medications Metabolized by Hepatic Cytochrome P450 Enzymes

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Educational Objectives:

At the conclusion of this presentation, participants should be able to:

1. Describe the studies conducted to assess the potential for pharmacokinetic drug interactions between selegiline transdermal system (STS) 20 mg and each of three CNS psychiatric medications metabolized by the hepatic cytochrome P450 enzymes.
2. Describe the results of the studies demonstrating the absence of pharmacokinetic drug interactions between alprazolam, risperidone and olanzapine and STS 20 mg.

Summary:

Introduction: Selegiline transdermal system (STS) is a transdermal formulation of selegiline developed to treat patients with MDD. STS avoids first-pass metabolism, thereby increasing selegiline bioavailability at CNS target sites. Computer-based homology models and *in vitro* assays with human hepatic microsomes and recombinant enzymes suggest that multiple cytochrome P450 (P450) isoforms (possibly 1A2, 2B6, 2C8, 2C9, 2C19, or 3A4) metabolize selegiline.[1-4]

Objective: Human studies were conducted to examine the potential for CYP450-related pharmacokinetic drug interactions between STS and each of 3 psychiatric medications that might be administered concomitantly with STS.

Methods: All major pharmacokinetic parameters were determined following treatment with STS 6mg/24hr or test agent (alprazolam, olanzapine, or risperidone) administered alone or in combination. Individual open-label, randomized studies were conducted using a Latin square, 3-sequence, crossover design administered to 6 treatment groups. Additional pharmacokinetic drug interaction studies were conducted with ketoconazole, ibuprofen, levothyroxine, and warfarin using a single sequence, 2- or 3-treatment study design.

Results: Alprazolam, risperidone, or olanzapine did not affect the pharmacokinetic properties of

STS 6mg/24hr. In addition, STS 6mg/24hr did not alter the pharmacokinetic properties of each of the test agents. Ketoconazole, ibuprofen, levothyroxine, or warfarin coadministration was also without effect on selegiline pharmacokinetics.

Conclusions: STS 6mg/24hr can be coadministered with alprazolam, risperidone, or olanzapine without the need for dose adjustments of either agent. Pharmacokinetic drug interactions were

also absent following ketoconazole, ibuprofen, levothyroxine, or warfarin treatment. Because multiple CYP450 pathways metabolize selegiline, use of STS 6mg/24hr is unlikely to result in pharmacokinetic drug interactions.

References:

1. Salonen JS: Comparative studies on the cytochrome p450-associated metabolism and interaction potential of selegiline between human liver-derived in vitro systems. Drug Metab Dispos 2003;31:1093-1102.
2. Taavitsainen P:Selegiline metabolism and cytochrome P450 enzymes: in vitro study in human liver microsomes. Pharmacol Toxicol 2000;86:215-221.

NR462 Tuesday, May 23, 3:00 PM - 5:00 PM

Clozapine Concentrations in Plasma and Leucocytes

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to better understand aspects of clozapine-induced agranulocytosis

Summary:

Objective: In order to explain clozapine-induced agranulocytosis immunological processes or direct toxic effects have been presented so far. However, more recent studies suggest that clozapine not yet metabolized is taken up by leucocytes and transformed by oxidative processes to apoptosis-inducing metabolites [1].

Methods: To clarify this hypothesis the concentrations of clozapine were measured in the plasma and the leucocytes of a patient suffering from delusional depression receiving clozapine for 8 weeks and developing clozapine-induced leucocytopenia, as well as in 10 patients receiving clozapine for a longer period of time without serious adverse side effects. Leukocytes were isolated by sedimentation on a Ficoll gradient. For the assessment of the clozapine concentrations in the plasma and the leucocyte fraction mass spectrometry was used.

Results: The patient developing leucocytopenia showed clozapine concentrations in the leucocytes about 8 times higher than the mean clozapine concentrations in the leucocytes in the group of 10 patients receiving clozapine without changes in the leucocyte count in the history (12.8 ng/ml versus 1.58 ± 1.39 ng/ml, range: 0.20-4.2 ng/ml; plasma-level-corrected clozapine concentrations in the leucocytes: 0.04 ng/ml versus 0.0067 ± 0.0048 ng/ml). However, the clozapine plasma concentrations showed no major difference (285 ng/ml versus 191± 154 ng/ml; dose-corrected clozapine plasma concentrations: 1.63 ng/ml versus 0.58 ± 0.42 ng/ml).

Conclusions: The results suggest that patients on risk of clozapine-induced leucocytopenia show increased clozapine concentrations in the leucocytes whereas the clozapine plasma concentration is in the therapeutic range. It is assumed that changes or abnormalities of the clozapine specific transporter system at the cell membrane might play a role in the development of clozapine-induced leucocytopenia and/or agranulocytosis [2].

References:

1. Iverson S et al.: Predicting drug-induced agranulcytosis ... Chem Biol Interact 2002; 142:175–199.
2. Henning U et al.: Uptake of clozapine into HL-60 promyelotic leukemia cells. Pharmacopsychiatry 2002; 35:90–95.

NR463 Tuesday, May 23, 3:00 PM - 5:00 PM

Comparative and Acute Efficacy and Tolerability of OROS and Immediate Release Formulations of Methylphenidate in the Treatment of Adults With ADHD

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that equipotent daily doses of once daily OROS MPH has similar efficacy and tolerability to that of TID administered IR MPH.

Summary:

Objective. The main aim of this study was to compare the safety and efficacy of equipotent doses of IR MPH administered TID to those of once daily OROS MPH. **Methods.**.Data from two independently conducted 6-week placebo controlled, randomized clinical trials of IR-MPH(tid) and of OROS-MPH were pooled to create three study groups: Placebo (N=116), IR-MPH(tid) (N=102) and OROS-MPH (N=67). Subjects were outpatient adults with ADHD between 19 and 60 years of age. To be included subjects had to satisfy full diagnostic criteria for DSM-IV ADHD based on clinical assessment and confirmed by structured diagnostic interview. **Results.** Eight-five percent (N=99) of placebo treated subjects, 77% (N=79) of the IR-MPH(tid) treated subjects, and 82% (N=55) of the OROS-MPH treated subjects completed the 6-week trial. Total daily doses at endpoint were 80.9±31.9 mg, 74.8±26.2 mg, and 95.4±26.3 mg in the OROS-MPH, IR-MPH(tid), and placebo groups, respectively. At endpoint, 66% (N= 44) of subjects receiving OROS-MPH and 70% (N=71) of subjects receiving IR-MPH(tid) were considered responders compared with 31% (N=36) on placebo an *a priori* definition of response of much or very much improved on the CGI *plus* more than a 30% reduction in symptoms on the AISRS. Both the IR-MPH(tid) and the OROS-MPH treated subjects were more likely to report dry mouth, decreased appetite, sleep difficulties and moodiness than were subjects treated with placebo. **Conclusion.** Comparison of data from two similarly designed, large, randomized, placebo-controlled, trials, showed that equipotent daily doses of once daily OROS MPH has similar efficacy and tolerability to that of TID administered IR MPH.

References:

1. Spencer TJ, Biederman J: Efficacy in a 6-month trial of methylphenidate in adults with ADHD. 49th Annual Meeting: Amer Acad Child Adol Psychiatry, San Francisco, CA, 2002.
2. Spencer TJ, Wilens T, Biederman J, Faraone AV, Ablon JS, Lapey K: A double-blind, crossover comparison of methylphenidate and placebo in adults with childhood-onset attention-deficit hyperactivity disorder. Arch Gen Psychiatry 1995; 52(6):434-443.

NR464 Tuesday, May 23, 3:00 PM - 5:00 PM

Comparative Efficacy of Atypical Antipsychotics in Youth With Bipolar Disorder

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that the study suggests that atypical antipsychotics reduce manic symptomatology in youth with Bipolar Disorder.

Summary:

Background: Childhood bipolar disorder is among the most severely disabling psychiatric conditions affecting children. It is associated with great severity of the illness (eg, psychosis, mixed mania, and high rates of aggression) and impairment. Because pediatric bipolar disorder has been assumed to be extremely rare or non-existent, very little is known about its treatment and, to date, there is no accepted therapeutic "gold standard". Yet, children with bipolar disorder are frequently treated with many medications with unclear efficacy and inadequate safety data. The goal of this study was to pool the data from our studies of atypical antipsychotics in the treatment of children with bipolar disorder(BPD) to make head-to-head comparisons of these compounds in a large sample.

Methods: Subjects were assigned to one of several identically designed trials. Each study consisted of 8-weeks of open-label monotherapy with an atypical antipsychotic (risperidone, quetiapine, ziprasidone, or olanzapine). Each subject met criteria for DSM-IV BPD I, DSM-IV BPD II, or BPD NOS, and were currently displaying manic, hypomanic, or mixed symptoms (with/without psychotic features) according to the DSM-IV based on clinical assessment.

Results: 101 subjects were enrolled (10.2±2.7 years of age, 67% male). At baseline all groups were markedly impaired according to the YMRS. Clinical ratings on the CGI indicate that the effect was strongest for risperidone, followed by ziprasidone, quetiapine, and olanzapine. There were moderately increased prolactin levels associated with risperidone, but prolactin was not elevated to a clinically significant level in any subject. Olanzapine was associated with marked increase in weight that was statistically significantly greater than the other groups.

Conclusions: This study suggests that atypical antipsychotics reduce manic symptomatology in youth with BPD. Future placebo-controlled, double blind studies of these compounds are warranted in this population.

References:

1. Biederman J, Mick E, Johnson MA, Wozniak J, Aleardi M, Spencer T, Faraone SV: A prospective open-label treatment of risperidone monotherapy in children and adolescents with bipolar disorder. J Child Adol Psychopharm 2004; in press.
2. Biederman J, Faraone SV et al.: Further evidence of unique developmental phenotypic correlates of pediatric bipolar disorder. J Affective Disorders 2004; 82(1):S45-S58.

NR465 Tuesday, May 23, 3:00 PM - 5:00 PM

An Open-Label Study of Divalproex Sodium Monotherapy in Youth With Bipolar Disorder

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to know more about the efficacy of divalproex sodium in the treatment of bipolar disorder in youth.

Summary:

Background: The purpose of this study was to evaluate the safety, tolerability and effectiveness of divalproex sodium monotherapy in the treatment of youth with bipolar disorder. Based on the adult clinical trial literature, we hypothesized that divalproex sodium would be a well tolerated and efficacious treatment for youth with bipolar disorder. **Methods:** This was an eight-week, open-label, prospective study of divalproex sodium monotherapy (847±486 mg/d) in 18 bipolar youth (manic, mixed, or hypomanic; 6-17 years old). Assessments included the Young Mania Rating Scale (YMRS) and Clinical Global Impressions-Improvement scale (CGI-I). Adverse events were assessed through spontaneous self-reports, vital signs weight monitoring, and laboratory analysis. Random regression models were used to conduct intention to treat (ITT) analyses with the last observation (LOC). Statistical significance was determined at $p<0.05$. **Results:** Seven of the 18 youth (39%) completed the study. Dropouts were due to lack of efficacy (N=3) or adverse effects (N=8). Divalproex sodium treatment was associated with clinically and statistically significant improvement in mean YMRS scores (-7.6±12.9, p=0.03). Using predefined criteria for improvement (Clinical Global Impressions Improvement -Mania score of ≤2 at endpoint), the response rate for manic symptoms was 59%. Adverse effects reported at the drop visit (not mutually exclusive) were GI complaints (N=2) anxiety (N=2) insomnia (N=1), sedation (N=1), depression (N=1), agitation (N=1), enuresis (N=1) and increased appetite (N=1). Increase in body weight was modest and not statistically significant (1.4±3.0 kg, p=0.08). **Conclusions:** Although the majority of subjects did not complete this 8-week trial of monotherapy, ITT analysis provides preliminary evidence that divalproex sodium may be efficacious in the treatment of pediatric bipolar disorder. Follow-up of these findings with controlled trials in this population is warranted.

References:

1. Biederman J, Faraone SV et al.: Further evidence of unique developmental phenotypic correlates of pediatric bipolar disorder. J Affective Disorders 2004; 82(1):S45-S58.
2. Wagner KD, Weller EB, Carlson GA, Sachs G, Biederman J, Frazier JA, Wozniak R, Tracy K, Weller RA, Bowden C: An open-label trial of divalproex in children and adolescents with bipolar disorder. J Am Acad Child Adol Psychiatry 2002; 41(10):1224-30.

NR466 Tuesday, May 23, 3:00 PM - 5:00 PM

Safety and Tolerability of Long-Term Treatment With Indiplon: Results of a Randomized 12-Month Study

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Educational Objectives:

The research data presented will contribute to the participant's understanding of the safety and tolerability of long-term treatment with indiplon in patients diagnosed with chronic primary insomnia.

Summary:

Introduction: There have been relatively few studies conducted to evaluate the safety of long-term treatment of insomnia. We summarize here the results of a long-term study of the safety of indiplon, a novel, α_1 sub-unit-selective, Gamma-aminobutyric acid $_A$ receptor modulator.

Methods: Adult patients (n=536) who met DSM-IV criteria for primary insomnia were randomized to 12 months of double-blind, as-needed, treatment with either indiplon 10 mg or 20 mg. Safety assessments included evaluation of adverse events, ECGs, clinical laboratory testing, and vital signs. Patients provided a global assessment of whether treatment was helping their insomnia.

Results: The 3 most frequent adverse events (incidence, median day of onset, median duration, respectively) on indiplon 10 mg were headache (11.8%; day 29; 8 days), back pain (7.9%; day 114; 23 days), and somnolence (7.9%; day 2; 29 days). The 3 most frequent adverse events on indiplon 20 mg were headache (8.7%; day 10; 5 days), URI (6.5%; day 180; 10 days), and nasopharyngitis (5.9%; day 136; 7 days). No dose-response effect was observed for adverse events. No clinically meaningful changes were observed in vital signs or ECG parameters, and there were

only isolated abnormal lab values. At month 2, study treatment was rated as helping insomnia by 80% of patients on indiplon 10 mg, and 85% of patients on indiplon 20 mg. These levels of were maintained through month 12. Frequency of indiplon dosing did not increase over time.

Conclusions: Long-term treatment with indiplon was found to be safe and well-tolerated; no unexpected adverse events occurred. Indiplon maintained high levels of patient-rated therapeutic effectiveness across 12 months of treatment with no increase in dosing frequency.

References:

1. Foster AC, Pelleymounter MA, Cullen MJ, Lewis D, Joppa M, Chen TK, Bozigian HP, Gross RS, Gogas KR. In vivo pharmacological characterization of indiplon, a novel pyrazolopyrimidine sedative-hypnotic. J Pharmacol Exp Ther 2004;311:547-559.
2. Simon GE, VonKorff M. Prevalence, burden, and treatment of insomnia in primary care. Am J Psychiatry 1997;154:1417-1423.

NR467 Tuesday, May 23, 3:00 PM - 5:00 PM

The Efficacy of Milnacipran in Panic Disorder: A Pilot Open Trial

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to compare the efficacy of this new drug (milnacipran) with the current drugs used in the treatment of Panic Disorder. Also, to know that drugs with both serotoninergic and adrenergic effect are effective in the PD treatment. Besides that, the present study intends to promote the discussion about the possibility of the involvement of different neurotransmitters in PD.

Summary:

Background: Milnacipran is a 5HT-noradrenalin reuptake inhibitor (SNRI). Venlafaxine, a medication of this same group that is proved to be efficient in the treatment of panic disorder (PD), has its effects primary by the 5HTergic inhibition, in contrast with the effect both 5HTergic and adrenergic of milnacipran.

Objective: The aim of this study was to evaluate the efficacy and effectiveness of milnacipran in the acute treatment of patients with PD.

Methods: Twelve eligible outpatients who met DSM-IV criteria for PD with or without agoraphobia, with 18 years old or more were included. Doses of milnacipran were initially of 25 mg, 2X/day, for 7 days and, then, 50 mg, 2X/day until the end of the study. The treatment outcome and PD severity were determined by Panic Disorder Severity Scale, Panic Inventory, Clinical Global Impression (CGI), and Hamilton Anxiety Scale. Data concerning adhesion to treatment and side effects were also obtained. At the beginning and the end of the study, subjects were evaluated for quality of life (WHOQOL-bref).

Results: Pharmacological treatment resulted in a clinically and statistically significant mean reduction in the CGI Severity score (4.17 (0.8) to 2.17(0.7), p=0,001). Remission (CGI≤2) was obtained in 66% of the sample. Significant improvement ($p<0.05$) was also noted in Hamilton Anxiety Scale, Agoraphobia and Anticipatory Anxiety. Regarding WHOQOL, we found a significant improvement ($p<0.05$) across treatment in all domains studied. Patients with a comorbid diagnosis of major depression had a lower remission rate

Conclusion: Although results may be influenced by the open nature of this pilot study and the small sample size, our findings suggest that milnacipran may be effective for the treatment of panic disorder and justify further research.

References:

1. Journal Article - Puozzo C: Pharmacology and pharmacokinetics of milnacipran. Int Clin Psychopharmacol 2002;17:25-35.
2. Journal Article - Bisserbe JC: Clinical utility of milnacipran in comparison with other antidepressants. Int Clin Psychopharmacol 2002; 17(suppl 1):43-50.

NR468 Tuesday, May 23, 3:00 PM - 5:00 PM

Combination of Antidepressants From Treatment Initiation for Depression

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Educational Objectives:

At the conclusion of this presentation, clinicians will become cognizant of the option which consists of using two antidepressants from treatment initiation of depression, a strategy which can help minimize side effects and may double the remission rate within a 6-week period when compared to using a single medication.

Summary:

Introduction. Remission rates using a single antidepressant are always below 50%. Augmentation strategies are often used following a first failed trial. In this study, two medications were used from treatment initiation in an attempt to improve treatment success.

Methods. Patients with a primary diagnosis of major depression (n=105) were randomized to receive for 6 weeks fluoxetine (20 mg/day), fluoxetine + mirtazapine (30 mg HS), bupropion (150 mg/day) + mirtazapine (30 mg HS), or venlafaxine (75 mg/day X 1 week, 150 mg/day X 1 week and 225 mg/day X 4 weeks) + mirtazapine (30 mg HS).

Results. The dropout rate (overall 15%) was approximately the same in the four treatment groups. The percentage of patients achieving remission (Hamilton depression score of 7 or less on the 17 item scale) was 25% in the fluoxetine group, and was significantly higher in the fluoxetine + mirtazapine group (52%) and in the venlafaxine + mirtazapine group (58%), but not quite so in the bupropion + mirtazapine group (46%).

Conclusion. These medication combinations from treatment initiation were well tolerated and produced a better outcome within a standard antidepressant trial duration.

References:

1. Nelson JC, Mazure CM, Jatlow PI, Bowers MB Jr, Price LH. Combining norepinephrine and serotonin reuptake inhibition mechanisms for treatment of depression: a double-blind, randomized study. Biological Psychiatry 55:296-300, 2004.
2. Blier, P. Medication combination and augmentation strategies in the treatment of major depression. In: The American Psychiatric Publishing Textbook of Mood Disorders. Eds: DJ Stein, DJ Kupfer, AF Schatzberg. American Psychiatric Publishing Inc, Wa.

NR469 Tuesday, May 23, 3:00 PM - 5:00 PM

The Pressor Effects of Oral Tyramine Following Treatment With the Selegiline Transdermal System

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Azzaro, Ph.D., Eva M. Kemper, Bryan Campbell, Pharm.D., Chad M. VanDenBerg, Pharm.D.

Educational Objectives:

At the conclusion of this presentation, participants should be able to:

1. Describe the multiple trials conducted to evaluate the pressor effects of oral tyramine following selegiline transdermal system (STS) administration.
2. Describe how the data support the recommendation that STS 20 mg can be administered without dietary tyramine restrictions.

Summary:

Introduction: The selegiline transdermal system (STS) was developed to overcome limitations of orally available MAO inhibitors (MAOIs), including the need for dietary tyramine restrictions. STS provides antidepressant concentrations of selegiline with reduced impact on the gastrointestinal MAO system.[1]

Objective: To evaluate the pressor effects of oral tyramine with concurrent STS administration in healthy volunteers.

Method: Multiple trials were conducted under a variety of experimental conditions; variables included STS dose (6mg/24hr to 12mg/24hr), duration of drug administration, dietary state (tyramine administration with and without food), and comparator MAOI drugs (oral selegiline and tranylcypromine). The endpoint was the amount of tyramine necessary to raise systolic blood pressure by 30 mm Hg (TYR30).

Results: In 2 crossover studies conducted in the fasted state, the mean TYR30 for STS 6mg/24hr was similar to oral selegiline (STS=385 mg versus oral selegiline=338 mg) and 20-fold greater than tranylcypromine (STS=270 mg versus tranylcypromine=10 mg). With longer exposure (33 days), the mean TYR30 for STS 6mg/24hr was reduced to 204 mg. Mean TYR30 values stabilized after extended exposure (>30 days) to STS at the highest dose (12mg/24hr), demonstrating achievement of pharmacodynamic steady-state. In this study, mean TYR30 was reduced to 95 mg, 72 mg, and 88 mg at 30, 60, and 90 days, respectively. Importantly, when tyramine capsules were administered with food, the mean TYR30 increased by 2.7-fold for STS 12mg/24hr, with the lowest individual TYR30 being 75 mg.

Conclusion: These results demonstrate a wide tyramine safety margin for STS (a high tyramine meal contains <40 mg[2]). With increasing dose and duration (up to 30 days), mean TYR30 is reduced. Nevertheless, these results, combined with the extensive clinical history of oral selegiline use without dietary tyramine restrictions, suggest that STS 6mg/24hr can be administered safely without dietary tyramine restrictions.

References:

1. Bodkin JA, Amsterdam JD: Transdermal selegiline in major depression: a double-blind, placebo-controlled, parallel-group study in outpatients. Am J Psychiatry 2002;159(11):1869-1875.
2. Walker SE, Shulman KL, Tailor SA, Gardner D: Tyramine content of previously restricted foods in monoamine oxidase inhibitor diets. J Clin Psychopharmacol 1996;16(3): 383-388.

NR470 Tuesday, May 23, 3:00 PM - 5:00 PM

A Combined Post-Hoc Analysis of Thyroid Function, Subsyndromal Symptoms, and Treatment for a Mood Episode From Two Placebo-Controlled, 18-Month Maintenance Studies in Bipolar I Disorder

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Educational Objectives:

At the conclusion of this presentation, the participant should be able understand patient response and tolerability to lamotrigine treatment.

Summary:

Objective: The effect of psychotropics on the hypothalamic-pituitary-thyroid axis and subsequent mood stability in long-term bipolar maintenance trials has not been studied.[1] Patients receiving lamotrigine (Ltg), lithium (Li) or placebo (Pbo) in two 18-month maintenance studies were examined with regard to treatment effect on both TSH and subsyndromal symptoms as well as the association between TSH and treatment for a mood episode.[2]

Methods: TSH at week 52 (±14 days) was compared across treatments and the percentage of visits from screening to week 52 with subsyndromal symptoms (HAM-D score 8 to 14 or MRS score 8 to 13). TSH values were also compared between patients with and without treatment for a mood episode within the first 52 weeks.

Results: All treatment groups had similar mean TSH values at screening (1.59-1.73). Mean TSH values at week 52 were 1.38±0.70 (range: 0.4-3.0), 2.56±1.86 (range: 0.2-8.4), and 1.38±0.80 (range: 0.2-3.9) for Pbo (n=22), Li (n=32), and Ltg (n= 55) groups, respectively (P<0.001 for Pbo and Ltg versus Li). Mean percentage of visits with subsyndromal symptoms were 20.9±27.3, 25.9±28.0, and 17.3±21.7 for Pbo (n=22), Li (n=32), and Ltg (n=55) groups, respectively. For patients that received treatment for a mood episode versus those that did not, mean TSH values were 1.36±0.74 (n=25) versus 1.44±0.78 (n= 29) for Pbo (*P*=0.687), 3.45±3.55 (n=18) versus 2.41±1.74 (n=35) for Li (*P*=0.143), and 1.37±1.00 (n=20) versus 1.43±0.88 (n=46) for Ltg (*P*=0.813).

Conclusions: TSH was significantly higher in the Li group at week 52, as compared to Ltg and Pbo. Although not statistically significant, a higher percentage of visits with subsyndromal symptoms were also observed for Li patients, and a higher TSH value was observed for Li patients who received treatment for a mood episode.

This study was supported by GlaxoSmithKline.

References:

1. Frye, M., Denicoff, K, Bryan B., Smith-Jackson, E., Ali, O., Luckenbaugh, D., Leverich, G., Post, R: Association between lower serum free T4 and greater mood instability and depression in lithium-maintained bipolar patients. Am J Psychiatry 1999;.
2. Goodwin et al.: A pooled analysis of 2 placebo-controlled 18-month trials of lamotrigine and lithium maintenance in bipolar I disorder. J Clin Psychiatry 2004; 65:432-441.

NR471 Tuesday, May 23, 3:00 PM - 5:00 PM

Effects of Depression on Cerebral Metabolism in Bipolar Disorder

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to discuss the changes in cerebral metabolism that result from bipolar depression.

Summary:

Objective: To determine cerebral metabolic changes in patients with bipolar depression compared to healthy control through the use of resting 18F-fluoro-deoxyglucose and PET (FDG-PET).

Method: The bipolar depressed group comprised 15 community-dwelling patients (mean age 36.1 years) with a history of bipolar disorder (six bipolar I and nine bipolar II) who were medication-free for two weeks prior to receiving a resting FDG-PET scan. The average Hamilton Depression Scale (HAM-D) score was 33.9 in patients. The healthy control group comprised 35 individuals (meant age 32.5 years). Arterial blood sampling was performed during the PET scan for the computation of absolute metabolic rates.

Results: Statistical Parametric Mapping (SPM2) analyses revealed increased normalized cerebral metabolism among depressed bipolar patients relative to controls in left superior and transverse temporal gyri (BA 22 and 41), right parahippocampal gyrus (BA 36), right putamen, left dorsolateral prefrontal cortex (BA 10), and right fusiform gyrus (all p's < .0001). The normalized metabolic data did not reveal any significantly decreased metabolism in depressed bipolar patients relative to controls. Analyses of the absolute metabolic data revealed decreased metabolic rates among depressed bipolar patients relative to controls in the right inferior frontal and precentral gyri, left cerebellum, and right anterior cingulate (BA 24), all p's < .0015. The absolute metabolic data did not reveal any significantly increased metabolism.

Conclusions: Our findings extend previous work that focused on treatment-resistant, mainly rapid-cycling bipolar inpatients. Among our sample of community-dwelling depressed bipolar patients we found normalized prefrontal and parahippocampal hypermetabolism but also absolute hypometabolism in the anterior cingulate.

References:

1. Ketter, T.A. et al. (2001). Effects of mood and subtype on cerebral glucose metabolism in treatment-resistant bipolar disorder. Biol Psychiatry, 49, 97-109.
2. Strakowski, S.M., et al. (2005). The functional neuroanatomy of bipolar disorder: a review of neuroimaging findings. Mol Psychiatry, 10, 105-16.

NR472 Tuesday, May 23, 3:00 PM - 5:00 PM

A Trial of Lamotrigine for Memory in Corticosteroid-Treated Patients

E. Sherwood Brown, M.D. *UT Southwestern Medical Center, 5323 Harry Hines Boulevard, Dallas, TX, 75390-8849*, Gary Stuard, M.S.W.

Educational Objectives:

At the conclusion of this presentation, the participant should be able understand patient response to lamotrigine treatment.

Summary:

Introduction: In humans and animals, corticosteroids have effects on memory. In prior research, we demonstrated deficits in declarative memory and hippocampal atrophy in patients receiving long-term therapy with prescription corticosteroids.[1] Additionally, we reported results of an open-label trial in which significant improvement in mood and declarative memory was observed in corticosteroid-treated patients given lamotrigine (a medication that is postulated to modulate glutamate release).[2] We now report findings from a placebo-controlled pilot study of lamotrigine in patients receiving corticosteroids.

Methods: 28 outpatients receiving prednisone therapy (≥7 mg/day for ≥ 6 months) were randomized to receive either 24 months of lamotrigine titrated to a maximum dose of 400 mg/day or placebo. Mood was assessed with the Hamilton Rating Scale for Depression (HRSD) and Young Mania Rating Scale (YMRS) and declarative memory with the Rey Auditory Verbal Learning Test (RAVLT).

Results: Participants consisted of 18 men and 10 women; mean age was 46±11 years; 22 were receiving prednisone following a renal transplant. The lamotrigine-treated group (n=16) showed significant improvement from baseline to exit on the RAVLT total words recalled (3.3±6.1 words, p=0.05). RAVLT scores did not change significantly in the placebo-treated group (0.7±11.3 words, p=NS). Between-group differences in RAVLT performance did not reach statistical significance. HRSD scores decreased significantly in the placebo (-3.5±5.1, p=0.04) but not lamotrigine (-1.6±7.2, p=NS) groups. YMRS scores did not change significantly in either group.

Conclusions: In this pilot study, significant improvement in declarative memory was observed in corticosteroid-treated patients receiving lamotrigine but not in those receiving placebo. However, in our small sample, between-group differences in declarative memory performance were not found. The change in declarative memory with lamotrigine does not appear to be related to change in mood symptoms. Larger trials of lamotrigine in this population are warranted.

Funded by NIH grant MH-01725, medication provided by GlaxoSmithKline.

References:

1. Brown ES, J Woolston D, Frol A, Bobadilla L, Khan DA, Hanczyc M, Rush AJ, Fleckenstein J, Babcock E, Cullum CM: Hippocampal volume, spectroscopy, cognition, and mood in patients receiving corticosteroid therapy. Biol Psychiatry 2004; 55: 538-45.
2. Brown ES, Frol A, Bobadilla L, Nejteck VA, Perantie DC, Dhillon H: Effect of lamotrigine on mood and cognition in patients receiving chronic exodogenous corticosteroids. Psychosomatics. 2003; 44: 204-8.

NR473 Tuesday, May 23, 3:00 PM - 5:00 PM

Abnormal Functional Circuits Mediating Episodic Memory in Major Depressive Disorder

Indira Tendolkar, Dr. Med. Sc. *6500 HB Nijmegen, The Netherlands*, Philip van Eijndhoven, M.D., Sara Pieters, M.S.C., Guido van Wingen, M.S.C., Robbert Jan Verkes, Ph.D., Jan Buitelaar, Prof. Dr.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize how the neural underpinnings of the neuropsychological core deficit of Major Depressive Disorder, i.e. episodic memory, can help identifying functional alteration of brain regions that may be involved in the pathogenesis of depression.

Summary:

Objective: Episodic memory, i.e. the ability to place a past event in its appropriate spatio-temporal context, is a neuropsychological core deficit of MDD (henceforth called depression). Though episodic memory performance improves during remission when structural abnormalities are not evident yet[1], it is unclear, whether episodic memory processes are mediated by the same or different brain regions compared to healthy controls. Functional MRI (fMRI) can reveal abnormal neuronal responses thereby tackling core regions of depression.

Method: Avoiding confounding effects of chronicity and medication, we investigated twelve unmedicated patients (mean age 35.4±10.5) in remission from their first depression and twelve matched controls. Subjects had to learn items embedded in a context (in this case pictures dyed in different colors) and later had to retrieve item information as well as context information (source memory)[2]. Standard whole head T2*-weighted EPI-BOLD fMRI data were acquired on a 1.5 T MR-scanner along with a T1-weighted MP-RAGE sequence for structural analysis. Image pre-

processing and statistical analysis was performed using the SPM2 software, including voxel-based morphometry (to exclude subjects with structural deficits).

Results: Behavioral performance did not differ between patients and controls so that differences in functional activation could not be related to a difference in memory. A second-level random effects analysis between both groups revealed no global differences of the hemodynamic response. However, the patients showed smaller activations during encoding and retrieval in the medial temporal lobe accompanied by a stronger activation of left prefrontal regions during retrieval.

Conclusions: Our results suggest a dysfunction of the medial temporal lobe (MTL) during episodic memory, which at least is partly compensated by prefrontally mediated processes. The functional alteration of the MTL may play an essential role in the pathophysiology of MDD because it is present at an early stage of the disease and during remission.

References:

1. Vythilingham M, Vermetten E, Anderson GM, Luckenbaugh D, Anderson ER, Snow J, Staib LH, Charney DS, Bremner JD: Hippocamapal volume, memory, and cortisol status in major depressive disorder: effects of treatment. Biol Psych 2004; 56:1101-1111.
2. Weis S, Specht K, Klaver P, Tendolkar I, Willmes K, Ruhlmann J, Elger CE, Fernández G: Contextual retrieval and item recognition are dissociated within the human medial temporal lobe. NeuroReport 2004; 18:2729-2733.

NR474 Tuesday, May 23, 3:00 PM - 5:00 PM

Quetiapine and Risperidone in the Treatment of Schizophrenia: A Short- and Long-Term, Non-Randomized Study

Fernando Canas, M.D. *Hospital, Department of Psychiatry, Cordoba 30, chalet 2, Colmenar Viejo, 28770, Spain*, Victor Perez, M.D., Monica Tafalla

Educational Objectives:

At the conclusion of the presentation, the participant should be able to better understand the effectiveness and tolerability profile of quetiapine and risperidone in the acute and long-term treatment of schizophrenia.

Summary:

Objective: Compare tolerability and effectiveness of Quetiapine (QUE) with Risperidone (RIS) in the acute and long term treatment of schizophrenia in the clinical practice setting.

Methods: Multicenter, prospective, non-randomized, comparative study. Patients ≥18, admitted to an acute unit with schizophrenia, schizophreniform or schizoaffective disorder (DSM-IV), were prescribed QUE or RIS within the first week (3:1 ratio). Evaluations: baseline, weeks 1 and 2, discharge and 6 and 12 months after. The study was approved by an Ethical Committee. Written informed consent was obtained from every subject. Statistical analysis: Chi square or t-tests.

Results: 466 patients (QUE:345; RIS:121) were included; 422 were discharged from the acute unit with the initial treatment (QUE:311; RIS:111). Withdrawals during the 12-month follow-up were similar in both groups (QUE:34.7%; RIS:33.3%). Mean doses were 719.6mg/d QUE and 8.0mg/d RIS at discharge, and 718.5mg/d QUE and 7.0mg/d RIS after 1 year.

Baseline characteristics were similar between groups with some exceptions: QUE group had more co-morbid mood disorders (23.5% versus 11.5%, p=0.033); previous hospitalizations (3.7±4.3 versus 2.7±3.6, p=0.009); and depressive symptoms on the CDSS (6.1±5.8 versus 4.9±4.9, p=0.027).

Table: Change from baseline in efficacy scales

At end of treatment, the proportion of patients with EPS was higher with RIS than QUE: 53.8% versus 15.3% (p<0.001). Sexual dysfunction was more frequent in RIS group males (p<0.05). Orthostatic dizziness was more frequent in QUE group (14.7% versus 6.7%, p=0.024). Incidence of somnolence was similar in both groups (33.0% for QUE and 35.8% for RIS; p=0.576).

Conclusions: Quetiapine and Risperidone have similar efficacy in the acute and long-term treatment of schizophrenia, although Quetiapine showed a more favourable EPS profile and less impact on males' sexual functioning.

References:

1. Cheer, S.M., Wagstaff, A.J.,. Quetiapine. A review of its use in the management of schizophrenia. CNS Drugs 2004;18:173-99.
2. Osser DN, Sigadel R,. Short-term inpatient pharmacotherapy of schizophrenia. Harv Rev Psychiatry 20019, 89-104.

NR475 Tuesday, May 23, 3:00 PM - 5:00 PM

An Open Label Follow-Up Study on Amisulpride in the Add-On Treatment of Bipolar I Patients

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Educational Objectives:

At the conclusion of this session, the participant should have acquired knowledge of the efficacy of amisulpride combination therapy for the treatment of patients with bipolar disorder.

Summary:

Atypical antipsychotics are widely used in the treatment of bipolar disorders. Amisulpride is an atypical antipsychotic that has been proven to be effective in treatment of schizophrenia, MDD and, more recently, acute mania. At the moment, however, no experimental study has assessed the effectiveness of this compound in mid-term maintenance therapy of bipolar disorders. The purpose of this study is to naturally determine the mid-term effectiveness of amisulpride in combination with standard treatments in 14 outpatients with bipolar I disorder who have shown inadequate responses to ongoing standard therapies. Due to dropping-out, the follow-up has been conducted on 11 patients for 11.7±8.2 months before (range 3-24) and 5.2±2.7 months after the introduction of amisulpride (range 3-9). Relapse rates before/during treatment with amisulpride have been calculated in accordance to an increase of 1 or more in Clinical Global Impression Scale-Bipolar Disorder (CGI-BP) score that was accompanied by a change in therapy or to an exacerbation of the symptoms who required a hospitalization. Mean CGI-BP scores have been calculated by comparing T-1 (3 months before the introduction of amisulpride), T0 (baseline) and T1 (3 months after the introduction of amisulpride) in the overall sample. A statistically significant decrease in the overall relapse rate was observed during the period of therapy compared with months previous to the introduction of amisulpride. The relative risk of relapse in the absence of it was 3.1 (χ2=4.2, P<0.05). Similarly, the rates of manic/mixed and depressive relapse were decreased but only manic ones reach the statistical significance (RR=5.3, χ2=5.2, P<0.02). This open-label study has demonstrated that mid-term therapy with amisulpride may benefit patients by improving global symptoms of bipolar disorder and reducing the rate of relapses. Large, randomized, controlled studies are needed to explore the benefits of adding long-term amisulpride to standard therapies for bipolar disorder.

References:

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NR476 Tuesday, May 23, 3:00 PM - 5:00 PM

Antipsychotics for Bipolar Disorder: McLean Hospital Inpatients, 2004

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Educational Objectives:

At the conclusion of this presentation, the participant will have a better understanding of current trends in the use of antipsychotic agents and concomitant psychotropics for inpatient treatment of bipolar disorder.

Summary:

Background: Since modern antipsychotics (APDs) had been recently FDA-approved for bipolar disorder (BPD), we examined their use for such patients.

Method: We analyzed medical records of 80 McLean Hospital DSM-IV BPD inpatients given APDs in mid-2004 for dosing and use of other psychotropics, and compared findings to similar 1998 [N=83] and 2002 [N=93] samples.

Results: Hospitalization of 80 BPD patients (aged 41.8 ± 13.5; 60% women) was for: depression (46%) > mania (29%) ≥ mixed-states (25%), lasted 10.7 days (vs. 13.6 in 2002, 22.4 in 1998), and was longest for mania. Usage ranked: risperidone > quetiapine > olanzapine >> aripiprazole > all others. Discharge doses averaged 312 ± 296 chlorpromazine-equivalent mg/day (higher with mania than depression). Depressed patients received more antidepressants and more total psychotropics. Concomitant mood stabilizers ranked: valproate > lithium > oxcarbazepine > lamotrigine > all others. In 2004, but not earlier, discharge prescriptions for APDs/patient (1.2) outnumbered lithium-plus-anticonvulsants (0.8). More BPD patients were discharged with ≥3 psychotropics in 2004 than 2002, and use of APDs as primary treatments doubled from 1998 to 2004. Use of olanzapine declined 2.4-fold from 1998 to 2004, and clozapine use decreased by 86% from its 2002 peak.

Conclusions: For hospitalized BPD patients, modern antipsychotics were used more than lithium, anticonvulsants, or older neuroleptics.

References:

1. Centorrino F, Fogarty KV, Sani G, Salvatore P, Cimbolli P, Baldessarini RJ: Antipsychotic drug use: McLean Hospital, 2002. Hum Psychopharmacol 2005; 20: 355-358.
2. Centorrino F, Fogarty KV, Salvatore P, Sani G, Cincotta SL, Hennen J, Guzzetta F, Talamo A, Saadeh MG, Baldessarini RJ: Use of combinations of antipsychotics: McLean Hospital inpatients, 2002. Hum Psychopharmacol 2005; 20: 485-492.

NR477 Tuesday, May 23, 3:00 PM - 5:00 PM

Prefrontal-Amygdalar Activation Changes Following Lamotrigine in Adolescents with Bipolar Depression

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to identify brain activation patterns that change following treatment with lamotrigine and the understand the effect of lamotrigine on adolescents with bipolar depression.

Summary:

Background: Adolescents with bipolar disorder (BD) have been shown to have abnormal prefrontal-subcortical activation patterns. Hypotheses regarding mood dysregulation in BD have centered around limbic overactivity with relative prefrontal underactivity during mood episodes. Lamotrigine (LTG) is effective in alleviating adult and adolescent bipolar depression. Therefore, we hypothesized that adolescents with bipolar depression successfully treated with lamotrigine would show decreases in amygdalar activation, and increases in prefrontal activation.

Methods: Eight subjects with BD, (4M/4F; 16.0±1.3 years), were scanned at baseline and then after 8 weeks of LTG treatment. Subjects were assessed weekly using the Children's Depression Rating Scale (CDRS). Mean final dose of LTG was 131 mg/day. We used a block design valenced visual stimuli task (using negative and neutral IAPS pictures). Data were acquired on a 3T GE Signa scanner and analyzed using SPM2. ROIs were defined in bilateral amygdala and dorsolateral prefrontal cortex (DLPFC) based on individual structural scans and prior loci of activation, consisting of 5 mm diameter spheres.

Results: All subjects were considered responders. Baseline CDRS was 53.0±10.6; Week 8 CDRS was 26.3±5.3. Group ROI activation patterns for negative-neutral pictures were computed for baseline and Week 8. Greater decrease in CDRS from baseline to Week 8 was correlated with greater decrease in right amygdalar activation (r=.91, p=.002). Similarly, at Week 8, CDRS score was positively correlated with bilateral amygdalar activation (r=.85, p=.007). DLPFC activation was not correlated with change in CDRS score, but was positively correlated with amygdalar activation in most comparisons.

Conclusions: As hypothesized, adolescents with BD treated with lamotrigine demonstrate less amygdalar activation when viewing negative stimuli as depressive symptoms improved. However, increases in prefrontal activation were not seen. This decrease in amygdalar activation may have been due to direct effects of lamotrigine, depressive symptom improvement, or practice effects.

References:

1. Chang KD, Saxena K, Howe M: Lamotrigine for the treatment of adolescent bipolar depression. In press.
2. Chang KD, Adleman N, Dienes K, Reiss AL: Anomalous prefrontal-subcortical activation in familial pediatric bipolar disorder: An fMRI Investigation. Arch Gen Psychiatry 2004; 61:781-792.

NR478 Tuesday, May 23, 3:00 PM - 5:00 PM

Quetiapine in Bipolar Disorder With Alcohol Dependence: A Pilot Study

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to :

1. recognize the relationship of alcohol dependence and bipolar disorder;

2. evaluate the evidence for the emerging role of atypical antipsychotics maintenance treatment in bipolar disorder with alcohol dependence

Summary:

Introduction: With the high rate of substance abuse comorbidity in bipolar disorder,pharmacological approaches targeting both mood stabilization and substance use relapse prevention merit special consideration. There is a paucity of studies of the atypical antipsychotic, quetiapine, in dually diagnosed bipolar disorder.

Objective: In the pilot study we evaluated whether quetiapine is efficacious in bipolar disorder with co-existing alcohol dependence.

Method: Our pilot study was open label. Dual diagnosis patients (DSM IV bipolar disorder and alcohol dependence) detoxified for at least 3 weeks completed structured clincial interviews prior to entering the study. During the 12-week study, the subjects participated in outpatient integrated care. For alcohol use, we used self-report alcohol use and urine drug screens and alcohol craving scale. The efficacy measures include: HAM-D (Hamilton Depression Rating Scale); YMRS (Young Mania Rating scale), BRRS (Brief Psychiatric Rating Scale), self-report Alcohol use Timeline method and alcohol craving score and CGI (Clinical Gobal Impression). Tolerability was monitored with treatment-emergent adverse events. Flexible dosage of quetiapine was used.

Results: We recruited 16 subjects (male: 10; female:6)diagnosed with bipolar disorder Type 1 (4/16) and Type 2 (12/16). Quetaipine average daily dosage was 400 mg. As compared to baseline values, bipolar disorder subjects demonstrated statiscally significant changes in YMRS, BPRS, HAM-D and CGI at the end of the 12 -week period (paired t-test, $p < 0.05$). Alcohol use outcome: number of drinking days and number of drinks per drinking day and alcohol craving score, showed similar statistically significant ($p< 0.05$) change from baseline to exit. The Dropouts (3/16) were unrelated to any serious adverse events.

Conclusion: The initial promising results with quetiapine in bipolar patients with alcohol abuse warrant controlled trials to establish the efficacy of quetiapine maintenance treatment in optimizing remission of bipolar disorder and alcohol relapse prevention.

References:

1. Goldberg JF, Grano JL, Leon Ac, Kocsis JH, Portera L (1999) A history of Substance abuse complicates remission from acute mania in biplar disorder. J. Clin. Psychiatry 60(11): 733-40.
2. Ketter TA,Want PW, Nowakowska C, Marsh WK NEw Medication Treatment Options for bipolar disorders. Acta Psychiat. Scand Suppl (422): 18-33.

NR479 Tuesday, May 23, 3:00 PM - 5:00 PM

Differential Outcome Study of Non-Mandated Addiction Treatment for Psychiatric Patients With Substance Use Co-Morbidity Mediating Role of Criminality

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Educational Objectives:

Towards the end of the presentation, the participant should be able to:

1. delineate the complex interrelationships of criminality, psychiatric disorders and addiction;
2. recognize criminality as a significant determinant in addiction treatment among dual diagnosis clients
3. appreciate the implications for integrating treatment with forensic rehabilitation services

Summary:

Introduction: The links between violence, criminality and addiction has been well recognized; however, few studies address the issue whether criminality influences the treatment outcome of patients with psychiatric and addiction disorders.

The objective of our study was to examine whether dual diagnosis patients with criminal history manifest differential treatment outcome from a dual diagnosis cohort with no criminal history.

Methods: The study was naturalistic. The data were extracted from 100 consecutive admissions to a multi-modal inpatient addiction program at a provincial psychiatric hospital. We used DSM IV to diagnosis substance use and psychiatric disorders. Criminal history was gathered from releant legal and correctional services. Outcome measures included random urine and blood drug and alcohol screen, retention rate, CGI (Clinical Global Impression score)and GAF (Global Assessment Functional Score).

Results: We found that 64% of the dual diagnosis patients had criminal offenses with assault being the commonest offenses. Polysubstance dependence (cocaine, marijuana, alcohol) with multiple relapse and intoxication episodes discriminated the forensic dual diagnosis (fDD) group from the non-forensic dual diagnosis group (nfDD). While mood disorders (bipolar disorder, dysthymia and unipolar depression) were equally distributed between the fDD and nfDD groups, the fDD group had higher rate of PTSD and anti-social personality disorder (chi square < 0.05). Outcome analysis showed that the fDD group (higher male/female ratio) had statistically significant higher dropout rate and positive urine toxicological screen and lowered GAF and CGI scores, when compared at baseline and exit ($p < 0.05$).

Conclusion: Our preliminary outcome study highlights the importance of criminality as mediating the addiction outcome among the dual diagnosis patients. Complex interrelationships of psychiatric disorders, criminality and addiction disorders implicate the necessity of integrating criminal justice rehabiliation services and psychiatric and addiction services to improve the outcome of forensic dual diagnosis clients.

References:

1. Brochu S, Guyon L, Desjardins L (1999) Comparative profiles of addicted adult populations in rehabilitation and correctional services J. Subst. Abuse treat. 16(2): 173-82.
2. Lamberti JS, Weisman RL, Schwarzkorpf SB, PRice N, Ashton RM, Trompeter J (2001) psychiatrc Quarterly 72(1): 63-77.

NR480 Tuesday, May 23, 3:00 PM - 5:00 PM

Safety and Maintenance of Effect of Orally Disintegrating Risperidone Tablets in Patients With Major Depressive Disorder, Bipolar Disorder, or Dementia: Results of an Open-Label Study

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Educational Objectives:

At the conclusion of this presentation, the participant should :

1) recognize that orally disintegrating risperidone tablets offer an alternative therapy to physicians struggling with compliance issues.

2) be aware that when patients are switched to orally disintegrating risperidone tablets from their previous risperidone formulation, clinical efficacy is maintained.

3) recognize stable patients and evaluate the appropriateness of transition therapy.

Summary:

Purpose: Safety and maintenance of clinical effect in subjects transitioned from compressed risperidone tablets to orally disintegrating risperidone tablets.

Method: Patients ≥ 18 years with DSM-IV diagnosis of MDD, Bipolar Disorder (BP) or Dementia (D) with baseline CGI-Severity

≤ 3 (mildly ill) and minimum 2 weeks prior risperidone therapy at a stable dose of 0.5, 1.0 or 2.0 mg/day were recruited and switched to equivalent doses of orally disintegrating risperidone tablets and assessed 4 weeks later. All MDD patients had been previously stabilized on an anti-depressant, most BP patients (16/21) were taking a mood stabilizer and most Dementia patients (13/20) were on a cholinesterase inhibitor.

Results: N=25 MDD, N=21 BP and N=20 Dementia . Mean age was 49.2+/-13.8 years (MDD), 45.7+/-13.2 (BP), 77.6+/-8.7 (D). Mean baseline CGI-S score was 2.5 +/- 0.7 (MDD), 2.3 +/- 0.7 (BP) and 2.8 +/- 0.4 (D) with a mean improvement observed at Week 4 of -0.13 +/- 0.45 (MDD), -0.17 +/- 0.4 (BP) and -0.3 +/- 0.6 (D) respectively. On a Visual Analogue Scale for acceptability of treatment, all diagnostic groups favourably rated orally disintegrating risperidone tablets, with patients rating acceptability at 6.4/10 (MDD), 8.2/10 (BP) and 7/10 (D) respectively. The most frequent AE reported was headache.

Conclusion: Orally disintegrating risperidone tablets offer an alternative, well-tolerated method of drug delivery with no evidence of symptom decompensation when transitioned from the previous risperidone formulation.

References:

1. Chue P, Welch, R., Binder, C., Acceptability and disintegration rates of orally disintegrating risperidone tablets in subjects with schizophrenia and schizoaffective disorder, Cdn. J. of Psych 2004 Oct;49(10):701-3.
2. Bachert C, El-Akkad, T, Patient preference and sensory comparisons of three intranasal corticosteroids for the treatment of allergic rhinitis; Annals of Allergy, Asthma, and Immunology 2002;89:292-297.

NR481 Tuesday, May 23, 3:00 PM - 5:00 PM

A Comparison of Bupropion XL With Venlafaxine XR for the Treatment of MDD: An Evaluation of the Relative Effects on Sexual Functioning, Efficacy, Safety, and Tolerability

Anita H. Clayton, M.D. *University of Virginia, Psychiatric Medicine, 2955 Ivy Road, Northridge Suite 210, Charlottesville, VA, 22903*, Michael E. Thase, Barbara Haight, Pharm.D., Marty C. Johnson, M.S., April E. Harriett, M.A., Nathalie E. Richard, M.S.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to describe differences between bupropion XL and venlafaxine XR in effects on sexual functioning, remission rates, and adverse effects in outpatients with major depressive disorder.

Summary:

Objective: Though bupropion has consistently demonstrated comparable antidepressant efficacy and tolerability advantages (less sexual dysfunction and sedation) in direct comparisons with the SSRIs, head-to-head comparisons with venlafaxine were lacking.

Methods: This 12-week, randomized, double-blind trial compared bupropion XL (150-450 mg/day) and venlafaxine XR (75-225 mg/day) in 342 adult outpatients with moderate-severe MDD with respect to sexual functioning, efficacy in MDD and safety. Sexual functioning was evaluated using the Changes in Sexual Functioning Questionnaire (CSFQ). Efficacy measures included the HAMD-17 (via IVRS), CGI-S, and

CGI-I. The primary endpoint was sexual functioning across weeks 5, 6, 9 and 12. MMRM methodology was used to account for missing data.

Results: Whereas sexual functioning improved in MDD patients treated with bupropion XL, it worsened in patients treated with venlafaxine XR. The differences were statistically significant at each time point beginning with week 2 (p≤.006) and across weeks 5, 6, 9, and 12 simultaneously (p=.005). Among the subgroup of patients with normal sexual functioning at baseline (77%), sexual functioning remained stable in the bupropion XL group while it significantly worsened in the venlafaxine XR group (p<.05 relative to baseline). Patients' depression improved comparably when treated with either bupropion XL or venlafaxine XR as measured by mean changes from baseline in HAMD-17 total score [-13.7 versus -12.8, respectively, 95% CI (-2.66, 0,87)] and CGI-S [-1.9 versus -1.8, 95% CI (-0.35, 0.15]; however, the remission rates (HAMD-17 ≤ 7 at Week 12) favored bupropion XL: 46% versus 33%, 95% CI (1.07, 3.46).

Conclusions: Improved sexual functioning was observed in MDD patients treated with bupropion XL while a decline in sexual functioning was observed in MDD patients treated with venlafaxine XR. Comparable improvements in efficacy for MDD as measured by HAMD-17 and CGI-S were observed with both treatments, although the remission rate was higher for bupropion XL.

References:

1. Thase ME, Haight BR, Richard N, et al. Remission rates following antidepressant therapy with bupropion or selective serotonin reuptake inhibitors: a meta-analysis of orignial data from 7 randomized controlled trials. J Clin Psychiatry 66(8):974-981.
2. Clayton AH, Wightman D, Horrigan JP, et al. A comparison of the effects on sexual functioning of bupropion XL, escitalopram, and placebo in outpatients with major depression. Poster presentation at the US Psychiatric & Mental Health Congress, San D.

NR482 Tuesday, May 23, 3:00 PM - 5:00 PM

Biological Evidence for Genetic Commonality Between Atypical Treatment-Emergent Weight Gain and Obese Phenotypes

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Educational Objectives:

At the conclusion of this session, the participant should be able to discuss common genetic findings between atypical antipsychotic treatment emergent weight gain and obese phenotypes and the link between a PKHD1 knockout mouse model and an obese phenotype.

Summary:

Objective: Atypical anti-psychotic treatment emergent weight gain continues to be an issue in the treatment of patients with schizophrenia and bipolar disorder. Clinicians must weigh both the efficacy and safety parameters of each atypical in selecting the appropriate therapy for each patient. Genetic variation, primarily single nucleotide polymorphisms (SNPs) associated with response have been identified[1]. Overlap between novel genetic contributors to atypical treatment emergent weight gain and an obese phenotype are demonstrated. This poster highlights the genetic overlap examined, an animal model, and offers a biological hypothesis on potential mechanisms at work.

Method: 3741 SNPs selected from a whole genome scan on 513 schizophrenic, schizoaffective and schizophreniform individuals with and without atypical treatment emergent weight gain were examined in a cohort of more than 300 parent-child trios collected for an obese phenotype. The Transmission Disequilibrium Test identified several novel genes. A mouse knockout model of one of the significant genes will be presented.

Results: Genes overlapping between these two populations include EPHA7, TOX and PKHD1. Biological investigation of these overlapping genes includes PKHD1. Mouse knockout models for PKHD1 display increased subcutaneous and intra-abdominal fat deposits as well as increased quantities of mesenteric fat in the PKHD1 mutant homozygote and heterozygote mice.

Conclusions: Several genes with reported cilia function have been linked with other conditions predisposing individuals to obese phenotypes.[2,3] These genetic differences effect cilia function have shown altered CSF flow and cilia-regulated ion transport. These observed phenotypes may suggest that a cilia-related mechanism contribute to obese phenotypes, including atypical-emergent weight gain. Additional pre-clinical and clinical studies need to be conducted to further elucidate the role of cilia function in conditions displaying obese phenotypes, including atypical-associated weight gain.

References:

1. Journal Article - Pan J, Wang Q, Snell WJ: Cilium-generated signaling and cilia-related disorders. Lab Invest 2005; 85: 452-463.
2. Journal Article - Sutters M and Germino GG: Autosomal dominant polycystic kidney disease: molecular genetics and pathophysiology. J. Lab. Clin. Med. 2003;141: 91-101.

NR483 Tuesday, May 23, 3:00 PM - 5:00 PM

A Randomized, Double-Blind, Placebo-Controlled Trial of Metformin (Glucophage®) for Weight-Gain Associated With Atypical Antipsychotics in Children and Adolescents

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Educational Objectives:

Participants will review date from a randomized clinical trial comparing the use of metformin (Glucophage®) in children and adolescents who gained weight on one of three atypical antipsychotics (olanzapine (Zyprex®), quetiapine (Seroquel®) or risperidone (Risperdal®)) and were treated with metformin (Glucophage®) along with dietary and activity counseling. At the conclusion of this presentation, the participants will be familiar with the use of metformin (Glucophage®) to stabilize weight gain, reduce body mass index and waist circumference in children on atypical antipsychotics. Participants will gain knowledge about how to dose metformin (Glucophage®), monitor safety labs and side effects.

Summary:

Purpose: To study the effects of metformin (Glucophage®) on body mass index (BMI=kg/m^2), weight, and waist circumference in children and adolescents who have gained excessive weight taking olanzapine (Olanzapine®), risperidone (Risperidone®), or quetiapine (Quetiapine®).

Background: Atypical antipsychotic effectively treat psychiatric illness in children and adolescents but weight gain and metabolic issues, including diabetes, complicate their use. A previous open label study in 19 children and adolescents showed significant mean weight loss after the addition of metformin (Glucophage®) while continuing atypical antipsychotics.

Methods: Thirty nine subjects, ages 10-17 years, who had gained > 10% of their pre medication body weight after up to one year's therapy with one of three atypicals were enrolled in a 16 week, randomized, double-blind trial with either placebo or metformin (Glucophage®) in addition to dietary and activity counseling with a registered dietician. Metformin was dosed 500mg PO QPM and increased stepwise weekly to 850mg BID. Anthropometric measures, fasting insulin, glucose, liver function tests and electrolytes were taken at regular intervals.

Results: Mean changes in metformin versus placebo, respectively, were statistically significant for weight (-0.13 +/- 2.9 versus +4.0 +/- 6.2 kg), BMI (-0.43 +/- 1.07 versus + 1.1 +/- 2.0 kg/m^2) and waist circumference (- 2.5 +/- 5.5 versus 3.6 +/- 6.9 cm) (all $p < .03$). Two subjects were diabetic at baseline and two placebo-treated subjects became diabetic either during the study or shortly thereafter. Placebo treatment was associated with the need for oral glucose tolerance tests based on insulin and glucose results, ($p < .025$). No serious adverse events or abnormalities in "safety" laboratories resulted from metformin(Glucophage®) treatment.

Conclusion: Metformin(Glucophage®) arrests weight gain, reduces BMI and waist circumference and is protective against hyperglycemia in children and adolescents on atypicals.

Key words: atypical antipsychotics, obesity, diabetes, metformin(Glucophage®)

Running title: metformin(Glucophage®) and atypical induced weight gain

References:

1. Patel NC, Crismon ML, Hoagwood K, et al. Trends in the use of typical and atypical antipsychotics in children and adolescents. J Am Acad Child Adolesc Psychiatry 2005;44(6):548-56.
2. Morrison JA, Cottingham EM, Barton BA. Metformin for weight loss in pediatric patients taking psychotropic drugs. Am J Psychiatry 2002;159(4):655-7.

NR484 Tuesday, May 23, 3:00 PM - 5:00 PM

Additional Data on the Safety and Tolerability of Bupropion Extended-Release: Newly Accumulated Data Extends Previous Findings in Placebo Controlled Clinical Trials

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Educational Objectives:

At the conclusion of this presentation the participant should be able to know the data on safety and tolerability of bupropion extended release in 2290 outpatients suferring from moderate to severe MDD.

Summary:

Method:

Safety and tolerability of the once-daily formulation of bupropion extended release (bupropion XL®) and comparators (either escitalopram or venlafaxine) are summarized from 5 placebo controlled 8-week studies in adult out patients with MDD. Two of the studies have just been completed.

Method:

Safety data from 2290 outpatients with moderate to severe MDD were pooled. Subjects were evaluated on a weekly or biweekly basis during the studies with questioning to elicit treatment-emergent adverse events. Blood pressure and heart rate were assessed at each study visit. Weight was assessed at baseline and study exit.

Results:

Adverse events resulted in premature discontinuation in the following proportion of patients: placebo 5%, bupropion XL 6%, and comparator 5%. The following adverse events occurred with incidence of at least 5% on drug and at a rate of >2X the rate observed with placebo- for bupropion: dry mouth, insomnia, and hyperhidrosis; for the comparator: nausea, fatigue, and hyper-

hidrosis. Non-fatal serious advents were reported by 7(<1%) placebo patients, 4(<1%) bupropion XL patients and 5(<1%) comparator patients during the treatment phase. One fatal SAE was reported in a placebo treated patient. There were no suicides or seizures in bupropion XL treated patients. Vital sign changes were similar across treatment groups, sustained changes in systolic blood pressure was reported in 3% of subjects in all groups, sustained diastolic changes was reported in 6% of bupropion XL and placebo patients and 7% in comparator patients, and sustained heart rate changes were reported in 7% of placebo subjects, 11% of bupropion patients and 8% of comparator patients.

Conclusion:

Bupropion extended-release was well tolerated as shown in this dataset of adult outpatients with MDD recently extended by two additional studies.

References:

1. data on file GSK.
2. data on file GSK.

NR485 Tuesday, May 23, 3:00 PM - 5:00 PM

Factors Related to Abnormal Brain Perfusion in Cocaine Addicts

Dartiu X. Da Silveira, Sr., Ph.D. *Federal University of Sao Paulo, Psychiatry, Rua Florida 320, Sao Paulo, 04565000, Brazil*

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the importance of neuroimaging in the assessment of cocaine users and to identify different patterns of abnormal brain perfusion through functional tomography.

Summary:

Objective: To evaluate the relationship between the pattern of cocaine use and cerebral perfusion among cocaine addicts.

Method: A sample of 30 cocaine addicts was studied using 99 m-Tc-HMPAO SPECT (single photon emission computed tomography with injection of 99 m-Tc-hexametilpropilenoamina-oxime). Their cerebral perfusion pattern was then compared with their pattern of cocaine use.

Results: Eighty percent of the sample presented some degree of impairment in brain perfusion, either focal or diffuse. There were no differences between sniffers and crack smokers regarding their perfusion patterns. No relationship could be established between the severity of SPECT abnormalities and the amount of drug consumption or period of abstinence. However, length of cocaine use did correlate with the severity of cerebral perfusion (Spearman correlation coefficient: r=0.45, p<0.05).

Conclusion: This study documents the high frequency of cerebral functional impairment in cocaine addicts and establishes the relationship between length of cocaine exposure and severity of perfusion abnormalities.

References:

1. Strickland TL, Mena I, Villanueva Meyer J, Miller BL, Cummings J, Mehringer CM, et al. Cerebral perfusion and neuropsychological consequences of chronic cocaine use. J Neuropsychi Clin Neurosci 1993;5:419-27.
2. Volkow ND, Mullani N, Gould KL, Adler S, Krajewski K. Cerebral blood flow in chronic cocaine users: a study with positron emission tomography. British J Psychiatry 1988,152:641-8.

NR486 Tuesday, May 23, 3:00 PM - 5:00 PM

Mirtazapine Add-on to Clozapine in Stabilized Schizophrenia: Effects on Cognition

Roberto Delle Chiaie, M.D. *Università di Siena, Istituto di Psicologia Clinica, via cicerone 44, roma, 00193, Italy,* Massimo Salviati, M.D., Samantha Fiorentini, M.D., Paolo Pancheri, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand the importance of using appropriate combinations of drugs (with special reference to mirtazapine) to improve cognitive performance in schizophrenic patients stabilised on atypical antipsychotic compounds. The goal of this challenge is to reduce negative symptoms, improving active psychosocial rehabilitation of the patient

Summary:

Objective. Among other atypicals, some lines of evidence indicated a superior effect of Clozapine on cognition in schizophrenia. Such effect has been hypothesised to be associated with the $\alpha 2$ presynaptic receptor blocking properties of the drug in prefrontal cortex and with the consequent enhancement of dopaminergic transmission in this area. This property is also shared by Mirtazapine, which showed to improve negative symptoms in stabilised Patients with Schizophrenia when added to ongoing treatments both with haloperidol or Clozapine. This study aimed at measuring specifically Mirtazapine's effects on cognition in Patients with Schizophrenia stabilised on Clozapine in order to assess if these effects are independent from its antidepressant activity.

Experiment Design. After baseline assessment with BPRS, HAM-D and the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS: measures cognition along 5 scales) we started 15 Patients with Schizophrenia previously stabilised on Clozapine (195± 58,16 mg/day) to an open label Mirtazapine add-on (30 mg/day). Patients were newly tested after 4 weeks.

Results. Independently from psychopathology ratings, all patients showed significant improvements in cognition, more pronounced on RBANS immediate and delayed memory subscales.

Conclusions. These data seem to indicate that Mirtazapine's α-2 receptor blocking properties may induce a specific improvement on cognition in schizophrenia.

References:

1. Hertel P, Fagerquist MV, Svensson TH: Enhanced cortical dopamine output and antipsychotic-like effects of raclopride by alpha-2 adrenoceptor blckade. Science 1999; 286: 105-107.
2. Berk M, Ichim C, Brook S: Efficacy of mirtazapine add on therapy to haloperidol in the treatment of negative symptoms of schizophrenia: a double bliund randomized placebo controlled study. Int Clin Psychopharmacol 2001, 16: 87-92.

NR487 Tuesday, May 23, 3:00 PM - 5:00 PM

Efficacy and Safety of Desvenlafaxine Succinate in the Treatment of Major Depressive Disorder

Nicholas DeMartinis, M.D. *University of Connecticut School of Medicine, 10 Talcott Notch Rd. East, MC-6415, Farmington, CT, 06030,* Paul P. Yeung, M.D., A. Richard Entsuah, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to discuss the efficacy, safety, and tolerability of DVS in the short-term treatment of major depressive disorder, including its effects on symptoms of pain associated with depression.

Summary:

Objective: Evaluate the efficacy and safety of an extended-release formulation of desvenlafaxine succinate (DVS), a novel 5HT-norepinephrine reuptake inhibitor (SNRI) in the short-term treatment of MDD.

Methods: Depressed outpatients (aged 18 to 65) were randomly assigned to DVS 100mg/day (n=114), 200mg/day (n=116), 400mg/day (n=113), or placebo (n=118) for 8 weeks. The primary efficacy variable was change from baseline in 17-item Hamilton Depression Rating Scale (HAM-D_{17}) score at the final on-therapy evaluation. The key secondary efficacy variable was the Clinical Global Impression-Improvement (CGI-I) score. The Visual Analog Scale-Pain Intensity (VAS-PI) was used to evaluate improvement in depression-related pain. Efficacy analyses were based on the ITT population on a LOCF basis.

Results: Reduction in HAM-D_{17} scores for the DVS 100-mg (-10.60) and 400-mg (-10.74) groups was significantly greater versus the placebo group (-7.65; P=0.0038 and P=0.0023, respectively); for the 200-mg group, the reduction was -9.63 (P=0.0764). All dose groups demonstrated significantly greater improvement on CGI-I versus placebo. Improvement in VAS-PI overall pain was significantly better for the 100-mg group versus placebo (P= 0.002). DVS was generally well tolerated; adverse events were consistent with the SNRI class.

Conclusions: DVS was effective and well tolerated in short-term treatment of MDD.

Funding: Wyeth Research

References:

1. Briley M: Clinical experience with dual action antidepressants in different chronic pain syndromes. Hum Psychopharmacol 2004; 19 Suppl 1:S21-S25.
2. Zajecka JM, Albano D: SNRIs in the management of acute major depressive disorder. J Clin Psychiatry 2004; 65 Suppl 17:11-8.

NR488 Tuesday, May 23, 3:00 PM - 5:00 PM

Ziprasidone in Major Depression: Superior to Antidepressants in Safety and Efficacy?

Daniel A. Deutschman, M.D. *Case Western Reserve University, Department of Psychiatry, 5571 Buring Ct, Fort Myers, FL, 33919*, Douglas H. Deutschman, Ph.D.

Educational Objectives:

At the conclusion of this educational activity, participants should be able to demonstrate an understanding of:

1.) the unique neurotransmitter reuptake transporter blockade activity of ziprasidone for the serotonin, norepinephrine and dopamine reuptake transporters

2.) the theoretical potential antidepressant efficacy that might derive from this reuptake transporter blockade

3.) the safety and adverse event burden of ziprasidone in the treatment of 143 patients with major depression.

4.) the efficacy of ziprasidone in the treatment of major depression (psychotic and non psychotic) in combination with an antidepressant (n=127) and alone (n=16) as monotherapy.

Summary:

Introduction: Ziprasidone may possess antidepressant efficacy as a consequence of its blockade of the pre-synaptic reuptake transporters for 5HT, norepinephrine and dopamine[1].

Objective: To determine if antidepressant efficacy can be demonstrated in patients with Major Depression on ziprasidone.

Method: Electronic medical records (Behavior2006) of all patients seen in a busy inpatient/outpatient private practice between 2001 and 2005 were reviewed for a diagnosis of Major Depression and two or more visits on ziprasidone. Efficacy was determined by change in GAF scores. Demographics, dose, duration and adverse events were noted.

Results:

8,892 patient records were reviewed; 4,801 Major Depression patients were identified. 143 patients on ziprasidone had two or more visits (total 1,553): 68 with psychosis and 75 without psychosis.

Demographics were similar in both, (means were): age 41 years, 94% Caucasian, 59% female.

Duration varied widely: 56 days psychotic, 18 days non-psychotic.

Ziprasidone dose in mg/d: 154 psychotic (25% on doses over 160) and 114 non-psychotic. 127 (89%) were on an antidepressant (concurrent therapy) and 16 (11%) were on ziprasidone alone (monotherapy).

All groups showed improvement ($p > 0.001$); differences between groups (not significant) were: 51 (44%) on an antidepressant when ziprasidone was begun improved (GAF increase 9), 50 (43%) begun on ziprasidone and an antidepressant simultaneously improved further (GAF increase13), and 14 (12%) on ziprasidone alone improved most (GAF increase16).

Adverse events were infrequent and mild; only sedation was greater than 2% (5%).

Discussion: This preliminary study is open label, naturalistic and retrospective (case review). Analysis of GAF scores suggests that the observed efficacy is

NOT a result of concurrent antidepressant use.

Conclusion: Ziprasidone appears safe and effective in Major Depression with and without psychosis both as monotherapy and in combination with traditional antidepressants. Efficacy may approach antidepressants; adverse event profile may be superior. Further study is warranted.

References:

1. Stahl SM and Shayegan DK. 2003. The psychopharmacology of ziprasidone: Receptor-binding properties and real-world psychiatric practice. J Clin Psych 64: 6-12 Suppl. 19, 2003.
2. Deutschman DH. 2005. Geodo (Ziprasidone) for Major Depression (psychotic/non-psychotic):Safe and Effective as Augmentation or Monotherapy. USPsych Cong., Nov. 9, 2005. Poster.

NR489 Tuesday, May 23, 3:00 PM - 5:00 PM

Sertraline's Side Effect Burden Is Significantly Lower Than Other SSRI/SSNRIs

Daniel A. Deutschman, M.D. *Case Western Reserve University, Department of Psychiatry, 5571 Buring Ct, Fort Myers, FL, 33919*, Douglas H. Deutschman, Ph.D.

Educational Objectives:

Sertraline's Side Effect Burden is significantly lower than that of the other SSRI/SSNRI's

Objectives

At the end of the poster presentation the participant should be able to demonstrate an understanding of: the impact of SSRI/SSNRI side effect burden, SEB, on patient adherence; the impact of non adherence on the long term course of affective and anxiety spectrum disorders; The three side effects that have the greatest impact on patient adherence: sexual side effects, weight gain, sedation

The rank order of SSRI/SSNRI agents in regards these effects: Citalopram and paroxetine, most burdensome, Escitalopram and venlafaxine intermediate, Fluoxetine, second least burdensome, Sertraline, least burdensome

The concept of choosing an SSRI/SSNRI on the basis of its side effect profile to: Facilitate patient adherence and Enhance patient clinical outcomes.

Summary:

Sertraline's Side Effect Burden is Significantly Lower Than Other SSRI/SSNRI's

Background: Side effect burden, SEB, dramatically effects patient adherence. Non adherence can adversely effect the course of affective and anxiety spectrum disorders. Significant SEB differences could guide physicians in choosing an antidepressant thereby improving patient outcomes.

Hypothesis: Can important differences in SEB be demonstrated between SSRI/SSNRI antidepressants?

Method: Electronic medical records (Behavior2006) of all patients (14,365) seen in a private inpatient/outpatient practice between 1998 and 2005 were screened for treatment with an SSRI/SSNRI. 7,807 had been on an SSRI/SSNRI; 3,646 of these had two or more visits. Demographics, dose, duration and SEB of the latter were assessed.

Results: Patient cohorts ranged from 624 for escitalopram to 1,226 for sertraline; ages from 3 to 100 years; 98% were Caucasian; 61% female; doses ranged from a fraction of the usual starting dose to as much as 100% of the FDA recommended upper level dose for a minority of patients; 52% on the agent for > 1 year. SEB (in order from most to least):

Sexual function - citalopram, paroxetine, venlafaxine, escitalopram, fluoxetine, and sertraline;

Weight gain - paroxetine, citalopram, venlafaxine, escitalopram, fluoxetine and sertraline;

Sedation - citalopram, escitalopram, paroxetine, venlafaxine, fluoxetine and sertraline.

Discussion: This was an open label, naturalistic, retrospective chart review. These data suggest that meaningful differences do exist in the SEB among SSRI/SSNRI. These data are predicted by Richelson's elucidation of the unique receptor profiles of each SSRI/SSNRI. These data could help guide physician decision making and contribute to patient long-term outcomes.

Conclusion: There are demonstrable differences among the SSRI/SSNRI's in regards to their SEB. Sertraline was least burdensome (followed by fluoxetine) while citalopram and paroxetine were most burdensome.. These data are preliminary. Further work on this subject is needed.

References:

1. Richelson, E. 2003. Interactions of Antidepressants with Neurotransmitter Transporters and Receptors and their Clinical Significance. J. Clinical Psychiatry 66 [Suppl 13] 5-12.
2. Deutschman, D.A. 2005. Are there Differences in Side Effect Burden Among the SSRI/SSNRI's.USPsych Congress November 9, 2005 Las Vegas, NV. Poster Presentation.

NR490 Tuesday, May 23, 3:00 PM - 5:00 PM

Caudate Metabolism is Increased and Less Sensitive to GABAergic Stimulation in Detoxified Male Alcoholic Patients

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Educational Objectives:

At the end of this presentation, the participant should be able to understand differences of the regional central glucose metabolism between alcoholic patients and normal controls as well as the influence of a lorazepam challenge in these groups.

Summary:

Objective: To test the hypothesis that the sensitivity of Gamma-aminobutyric acid ergic systems is reduced in alcohol dependence, we investigated the regional cerebral glucose metabolism (rCGM) before and after administration of lorazepam in male detoxified alcoholics.

Methods: Placebo or lorazepam (30μg/kg body weight), respectively, was injected intravenously 15 min prior to tracer injection. Mean global cerebral activity parametric t-maps were computed on a voxel-by-voxel basis using SPM99.

Results: RCGM in the baseline condition was significantly higher in the bilateral caudate in detoxified alcoholics compared to normal controls. After lorazepam administration, both groups showed a significant increase of the rCGM in the bilateral caudate head in comparison to the baseline condition. However, the difference between alcoholics and the normal controls was reduced in the lorazepam condition compared to baseline due to a less pronounced response to lorazepam in the alcoholic patients. In addition, lorazepam administration reduced rCGM in the bilateral thalamus in both groups.

Conclusions: Our hypothesis that the response to a lorazepam challenge is blunted in detoxified alcoholics could be confirmed. The differences in caudate and changes in thalamic metabolic activity point to disturbances of subcortical networks in alcoholism. It remains to be determined whether these abnormalities persist after longer periods of abstinence and whether these markers are related to relapse risk. Further studies with this paradigm in larger samples of well-defined high-risk populations are needed to clarify these questions.

References:

1. Schreckenberger M, Lochmann M, Mann K, Siessmeier T, Buchholz HG, Bartenstein P, Gründer G. The thalamus as the generator and modulator of EEG alpha rhythm: a combined PET/EEG study with lorazepam challenge in humans. Neuroimage 2004; 22:637-44.
2. Volkow ND, Wang GJ, Overall JE, Hitzemann R, Fowler JS, Pappas N, Frecska E, Piscani K: Regional brain metabolic response to lorazepam in alcoholics during early and late alcohol detoxification. Alcohol Clin Exp Res 1997; 21:1278-84.

NR491 Tuesday, May 23, 3:00 PM - 5:00 PM

Symptom Response and Remission in Insomnia: Analysis of How Various Criteria Perform

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Educational Objectives:

The research data presented will contribute to the participant's understanding of how to define symptomatic response and remission when treating patients diagnosed with primary insomnia.

Summary:

Objective: Response and remission are the two most commonly utilized measures of outcome in treatment studies of many psychiatric disorders, yet consensus regarding such criteria in the treatment of insomnia are lacking. The goal of this analysis was to test how various response and remission criteria for insomnia perform with respect to one another.

Methods: Month 1 efficacy data were analyzed from a prospective, double-blind, placebo-controlled trial utilizing indiplon 10 mg and 20 mg. Response and remission were evaluated using the following 4 outcome measures: (1) the 7-item, Investigator Global Rating of Change (IGR-C); (2) the self-administered 7-item Insomnia Severity Index (ISI); (3) normative values for sleep onset and total sleep time from a community survey (Lichtstein et al, 2004); and (4) no longer meeting insomnia severity criteria required for study entry, consisting of latency to sleep onset >45 mins, wake time after sleep onset >45 mins, and total sleep time <330 mins).

Results: At Month 1, the 2 candidate responder criteria yielded the following response rates: IGR-C <2 (indiplon 10 mg, 45% versus indiplon 20 mg, 58% versus PBO, 23%), and ISI-total score <15 (indiplon 10 mg, 69% versus indiplon 20 mg, 70% versus PBO, 53%). At Month 1, the 4 remission criteria yielded the following remission rates: IGR-C=1 (indiplon 10 mg, 18% versus indiplon 20 mg, 28% versus PBO, 8%); no longer meeting insomnia severity criteria for study entry (indiplon 10 mg, 32% versus indiplon 20 mg, 33% versus PBO, 17%); ISI-total score <10 (indiplon 10 mg, 36% versus indiplon 20 mg, 46% versus PBO, 22%); and return to community norm levels of sleep (indiplon 10 mg, 29% versus indiplon 20 mg, 25% versus PBO, 12%).

Conclusions: Empirical data provide an important first step for establishing consensus clinical criteria for response and remission in the treatment of insomnia.

References:

1. Frank E, Prien RF, Jarrett RB et al. Conceptualization and rationale for consensus definitions of terms in major depressive disorder. Remission, recovery, relapse, and recurrence. Arch Gen Psychiatry 1991;48:851-855.
2. Lichstein KL, Durrence HH, Riedel BW, Taylor DJ, Bush AJ. Epidemiology of Sleep. Lawrence Erlbaum Assoc, Mahwah, NJ, 2004.

NR492 Tuesday, May 23, 3:00 PM - 5:00 PM

Atypical Antipsychotics and Pituitary Neoplasms in the WHO Database

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Educational Objectives:

1. To review the links between dopamine antagonism and pituitary adenoma cell proliferation
2. To present research data on pituitary neoplams in atypical antipsychotic users in the WHO database

Summary:

Background: Hyperprolactinemia is an important adverse effect of potent D2 antagonists and preclinical studies have linked D2 blockade with pituitary adenoma formation. These findings prompted us to analyze the WHO database.

Methods: We analyzed the WHO adverse drug reactions (ADR) database focusing on adverse event reports of pituitary tumors (benign and not otherwise specified) for atypical antipsychotics (clozapine, risperidone, olanzapine, ziprasidone, quetiapine, aripiprazole) and haloperidol.

Results: A total of 64 reports of pituitary tumor ADRs were linked to the 7 antipsychotics of which 44 (69%) were linked to risperidone. The majority occurred in women. There were 4 reports with haloperidol, 5 with ziprasidone, 7 with olanzapine, 3 with clozapine, 1 with quetiapine and none with aripirazole. Relative to total number of ADRs, risperidone had the highest reporting ratio for tumors (1:382) followed by ziprasidone (1:504). Haloperidol and olanzapine were intermediate whereas clozapine and aripiprazole had the lowest relative reporting ratios. Six reports were associated with visual disturbances and one report was associated each with headache and convulsion.

Conclusions: Treatment with potent D2 blocking antipsychotics may be associated with newly diagnosed pituitary tumors. Although analyses of spontaneous adverse events is limited by reporting and detection biases, these findings taken together with preclinical carcinogenicity studies and clinical trial data suggest a possible causal relationship. Clinicians should consider an anterior pituitary adenoma in patients receiving antipsychotics who experience severe hyperprolactinemia, galactorrhea, gynecomastia or unexplained visual symptoms.

References:

1. Cristina C et al. Increased pituitary endothelial growth factor-a in dopamine D2 receptor knockout female mice. Endocrinology 2005; 146 (7):2952-2962.
2. Haddad PM, Wieck A. Antipsychotic induced hyperprolactinemia. Drugs 2004;64(20) 2291-2295.

NR493 Tuesday, May 23, 3:00 PM - 5:00 PM

Aripiprazole in the Acute Treatment of Schizophrenia: A Prospective Naturalistic Study in the Inner-City Hospital Setting

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to consider the benefits and risks of using aripiprazole as antipsychotic monotherapy in acutely psychotic patients with schizophrenia. Aripiprazole has proved effective in the treatment of chronic, stable schizophrenia, but its effectiveness in the acute hospital setting to treat severely psychotic patients is unclear.This poster describes the findings of a small (n=10) prospective naturalistic study on the use of aripiprazole to treat actively psychotic patients with schizophrenia in a busy inner-London acute psychiatric unit. Most patients (70%) responded within 4 weeks to aripiprazole treatment (15-30 mg daily), which was well tolerated and significantly reduced psychotic symptoms after 2 weeks. Side effects were mostly mild and transient, and included extrapyramidal symptoms and also neutropenia in an HIV-positive patient. Aripiprazole also remarkably attenuated dyskinetic movements in a patient with tardive dyskinesia.

Summary:

Aripiprazole in the acute hospital treatment of male, actively psychotic patients with schizophrenia

Objective: Aripiprazole, a novel atypical antipsychotic that acts as a partial dopamine-2 agonist, has proved therapeutically effective in chronic schizophrenia. This naturalistic study assessed its effectiveness in the hospital setting to treat acutely psychotic patients.

Method: Ten actively psychotic, male schizophrenic patients admitted to our acute unit (median age 36 years; median duration of illness 30 months; 48.8±8.2 BPRS baseline score, mean ± s.d, range 40-65) received aripiprazole monotherapy orally (15-30 mg daily) for at least 4 weeks. Five had an associated substance abuse disorder. One patient who was HIV-positive also had severe tardive dyskinesia.

Results: Most (n=7) responded to aripiprazole, which was well tolerated and ameliorated psychotic symptoms after 2 weeks (BPRS 35.4± 15.6; p=0.003). At 4 weeks, BPRS mean score of the six responders who completed treatment was 16.0 ± 12.2 (p= 0.0001). Patients on aripiprazole did not require benzodiazepine tranquilization any more frequently or at higher doses than those receiving other antipsychotics. Transient side effects included extrapyramydal symptoms (EPS, n=1) and neutropenia (n=1) in the HIV-positive patient, who responded to aripriprazole but whose treatment was discontinued. Aripiprazole remarkably attenuated his dyskinetic movements after two weeks.

Conclusions: The patient group was fairly representative of the male population requiring acute admission for treatment of psy-

chotic disorders. Results showed that aripiprazole can be safely and effectively employed to treat severely psychotic patients with schizophrenia. Its mode of action may pose a risk of EPS to some patients, but it may also prove of therapeutic benefit in disorders other than schizophrenia alone that are also associated with dopamine dysfunction. These may include tardive dyskinesia and possibly other extrapyramydal disorders. The full range of adverse reactions associated with its use, including the risk of drug-induced neutropenia, requires further scrutiny.

References:

1. Kasper S, Lerman N, McQuade RD, et al: Efficacy and safety of aripiprazole vs. haloperidol for lomg-term maintenance treatment following acute relapse of schizophrenia. Int J Neuropsychopharmacology 2003; 6:325-327.
2. Pigott TE, Carson WH, Saha AR, et al: Aripiprazole for the prevention of relapse in stabilized patients with chronic schizophrenia: a placebo-controlled 26-week study. J Clin Psychiatry; 64:1048-1056.

NR494 Tuesday, May 23, 3:00 PM - 5:00 PM

Cortisol Hypersecretion in Unipolar Major Depression With Melancholic and Psychotic Features: Dopaminergic, Noradrenergic, and Thyroid Correlates

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that hypercortisolemia (as reflected by cortisol non suppression to the dexamethasone supression test) in unipolar melancholic and psychotic depressed patients is associated with dysfunction of dopaminergic, noradrenergic and thyroid systems.

Summary:

Background: Evidence supports that hyperactivity of the HPA axis has a pivotal role in the psychobiology of severe depression. It has been hypothesized that hypercortisolemia may underlie abnormalities in catecholamine and thyroid systems.

Methods: Hormonal responses to DST, apomorphine test (a dopamine receptor agonist), clonidine test (an alpha 2-adrenoreceptor agonist) and 8 AM and 11 PM protirelin (TRH) tests were measured in 18 drug-free inpatients with a DSM-IV diagnosis of severe MDD with melancholic and psychotic features showing cortisol nonsuppression following dexamethasone and 23 matched hospitalized healthy controls.

Results: Compared with controls, patients showed (1) lower adrenocorticotropin and cortisol response to apomorphine ($P<0.015$ and $p<0.004$ respectively), (2) lower growth hormone response to clonidine ($P=0.001$), and (3) lower responses to TRH:11 PM maximum increment in plasma thyrotropin level ($P=0.006$) and the difference between 11 PM and 8 AM maximum increment in plasma thyrotropin values ($P=0.0001$).

Conclusions: Our findings, in a subgroup of unipolar depressed inpatients with psychotic and melancholic features, are compatible with the hypothesis that chronic elevation of cortisol may lead to dopaminergic, noradrenergic and thyroid dysfunction.

References:

1. Mokrani MC, Duval F, Crocq MA, Bailey P, Macher JP. Multihormonal responses to apomorphine in mental illness. Psychoneurendocrinology 1995;20:365-375.
2. Duval F, Mokrani MC, Crocq MA, Bailey P, Diep TS, Correa H, Macher JP. Dopaminergic function and the cortisol response to dexamethasone in psychotic depression. Prog Neuro-Psychopharmacol Biol Psychiat 2000;24:207-2253.

NR495 Tuesday, May 23, 3:00 PM - 5:00 PM

HPA, HPT, Dopaminergic, and Noradrenergic Abnormalities in Schizoaffective Disorder

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that patients with schizoaffective disorder show decreased pituitary TRH receptor activity, decreased pituitary D2 activity, increased HPA axis activity, and decreased alpha2-noradrenergic function.

Summary:

Background: The aim of this study was to assess hypothalamic-pituitary dopaminergic (DA), noradrenergic (NA), thyroid (HPT) and adrenal (HPA) activity in schizoaffective disorder. Method: Hormonal responses to 8 AM and 11 PM protirelin (TRH) tests, DST, apomorphine test (APO; a DA receptor agonist) and clonidine test (CLO; an alpha 2-adrenoreceptor agonist) were measured in 13 untreated male inpatients with DSM-IV schizoaffective disorder and 13 matched hospitalized healthy controls. Results: Compared with controls, patients showed 1) lower responses to TRH (11 PM-ΔTSH and $\Delta\Delta$TSH [i.e. difference between 11 PM-ΔTSH and 8 AM-ΔTSH] ($p<0.02$ and $p<0.0005$ respectively); 2) higher post-dexamethasone cortisol values ($p<0.02$); 3) lower APO-induced PRL suppression ($p<0.05$); 4) and lower growth hormone (GH) response to CLO ($p<0.001$). Conclusion: Our results suggest that decreased pituitary TRH and DA-D2 receptor function (possibly secondary to increased TRH and DA release, respectively), together with increased HPA axis activity and decreased alpha 2-noradrenergic function characterize untreated male schizoaffective patients.

References:

1. Mokrani MC, Duval F, Crocq MA, Bailey P, Macher JP. Multihormonal responses to apomorphine in mental illness. Psychoneurendocrinology 1995;20:365-375.
2. Duval F, Mokrani MC, Crocq MA, Bailey P, Diep TS, Correa H, Macher JP. Dopaminergic function and the cortisol response to dexamethasone in psychotic depression. Prog Neuro-Psychopharmacol Biol Psychiat 2000;24:207-2253.

NR496 Tuesday, May 23, 3:00 PM - 5:00 PM

Chronic Paroxetine or Venlafaxine Administration to Mice Exposed to a Chronic Stress Model

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Educational Objectives:

At the conclusion of this presentation, the participants should be able to recognize the role of GABA in depression through an animal model of depression. They will also recognize the effect of alteration of GABA content by long-term antidepressant treatment with either paroxetine as one of the selective serotonin re-uptake inhibitors [SSRIs] or venlafaxine as a serotonin-norepinephrine re-uptake inhibitor [SNRIs] in the frontal cortex (F.Cx) as a brain region crucial for the control of emotion and cognition obtained from mice exposed to chronic mild stress (CMS)-induced anhedo-

nia. Moreover, they will recognize the long-term behavioral changes of the CMS without and with antidepressant treatment.

Summary:

Introduction: The role of Gamma-aminobutyric acid in mood disorders and its interactions with 5-HT and NE systems is worthy of further study. Many studies reported that plasma Gamma-aminobutyric acid levels are relatively reduced in depressed patients. *Methods:* The present study investigated the alteration of Gamma-aminobutyric acid content by long-term antidepressant treatment with either paroxetine as one of the selective 5HT re-uptake inhibitors [SSRIs] or venlafaxine as a 5HT-norepinephrine re-uptake inhibitor [SNRI] in the frontal cortex (F.Cx) as a brain region crucial for the control of emotion and cognition obtained from mice exposed to chronic mild stress (CMS)-induced anhedonia. The long-term behavioral changes of the CMS without and with antidepressant treatment were also tested using the forced swimming test (FST). *Results:* The results of the present study demonstrated the reversal of anhedonia after 3 weeks intraperitoneal (i.p). administration of 1 and 8 mg/kg/day paroxetine and venlafaxine respectively to male albino mice continuously exposed to CMS protocol. Furthermore, the observation suggested that venlafaxine seems to be more efficacious than paroxetine in long-term behavioral changes recorded by the FST on tested groups. Additionally, there was a highly significant ($P<0.001$) increase in the Gamma-aminobutyric acid content of the FCx of mice exposed to chronic mild stress-induced anhedonia. *Conclusion:* The present study have suggested that Gamma-aminobutyric acid levels may be decreased in an animal model of depression and its reversal together with the behavior improvement by either paroxetine or venlafaxine could support the hypothesis that modification in Gamma-aminobutyric acid ergic activity in mood disorders may complement the monoaminergic and serotonergic theories, proposing that the balance between multiple neurotransmitter systems may be altered in these disorders.

References:

1. Delgado P.L., Price L.H., Heninger G.R., Charney D.S: Neurochemistry of affective disorders. In Handbook of Affective Disorders, edited by Paykel E.S, New York, Churchill Livingston, 1992, pp 219'253.
2. Blier P: Norepinephrine and selective norepinephrine reuptake inhibitors in depression and mood disorders: their pivotal roles. J. Psychiatry Neurosci., 2001; 26: S1'S2.

NR497 Tuesday, May 23, 3:00 PM - 5:00 PM

Cognitive Function and Acute Sedative Effects of Risperidone and Quetiapine in Patients With Stable Bipolar I Disorder: A Randomized, Double-Blind, Crossover Study

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to assess the differential effects of risperidone and quetiapine on cognitive function and treatment-induced sedation in patients with stable bipolar I disorder.

Summary:

Background: A double-blind 2x2 crossover study compared effects of risperidone and quetiapine on cognition and sedation in adults with stable bipolar I disorder (BPI).

Methods: At each of two 2-day study periods, half of patients were randomized to treatment sequence risperidone-quetiapine and half to quetiapine-risperidone. Patients received 2mg of risperidone with dinner on day 1, or 100mg of quetiapine with dinner on day 1 and 100mg with breakfast on day 2. Patients were tested at 10am on day 1 (baseline assessment) and at 10am, 12:30pm and 3pm on day 2 (post-dose assessments) of each study period. A neurocognitive composite score (NCS) was derived from 8 computerized tests of processing speed, attention, working memory, executive function, and declarative memory. Patients also rated treatment effects on fatigue (sedation) and vigor.

Results: Both periods were completed by 28 of the 30 patients. BPI was in full remission in 26 patients and in partial remission in 2. Between-treatment differences in NCS were significant ($P<0.05$) at all post-dose assessments, showing better cognitive functioning after risperidone compared to quetiapine (overall standardized effect size =1.05). These differences reflected relative performance declines following quetiapine, maximally at 10am and 12:30pm post-dose assessments. Significant advantages for risperidone relative to quetiapine were found in specific cognitive domains comprising processing speed, attention, working memory, and declarative memory. Quetiapine treatment was associated with significantly more fatigue and less vigor compared with risperidone ($P<0.05$ at the 10am and 12:30pm time points). Adverse events were reported by more patients after quetiapine than risperidone ($P<0.05$); somnolence was reported in 9 patients after risperidone and 24 after quetiapine. Conclusions: Large differences between risperidone and quetiapine were found on neurocognitive function and sedation in patients with BPI following initial treatment. These effects are of a magnitude expected to impact everyday functioning and compliance with continued treatment.

References:

1. Khanna S, Vieta E, Lyons B, et al. Risperidone in the treatment of acute mania: double-blind, placebo-controlled study. Br J Psychiatry 2005;187:229-234.
2. Smulevich AB, et al. Acute and continuation risperidone monotherapy in bipolar mania: a 3-week placebo-controlled trial followed by a 9-week double-blind trial of risperidone and haloperidol. Eur Neuropsychopharmacol 2005;15:75.

NR498 Tuesday, May 23, 3:00 PM - 5:00 PM

Comparing ETRANK, MMRM and LOCF Methods of Analysis in 18 Placebo-Controlled Venlafaxine Clinical Trials for the Treatment of Major Depressive Disorder

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Educational Objectives:

At the conclusion of this presentation, the partcipant should be able to:

1. Discuss different analytical methods and their applications
2. Assess the differences between MMRM, ETRANK and LOCF analyses
3. Compare the MMRM and ETRANK analysis methods with the more traditional LOCF method in all the RCTs where LOCF was the *a priori* analytical method

Summary:

Objectives: To compare mixed-model repeated measure (MMRM) and ETRANK analyses with last observation carried forward (LOCF), the *a priori* analysis of all phase II and III placebo-controlled randomized controlled trials (RCTs) of venlafaxine (Effexor ®) therapy of MDD.

Methods: This analysis used LOCF, MMRM, and ETRANK methods; the dependent variable was the 17-item Hamilton Ratings Scale for Depression ($HAM\text{-}D_{17}$) change from baseline. Re-

mission (HAM-D_{17} ≤7) also was analyzed using LOCF_Logistic Regression and Glimmix MMRM analysis.

Results: Two thirds of the 18 LOCF analyses revealed significant drug-placebo differences compared with 56% for MMRM and 76% for ETRANK. LOCF comparisons (27.8%) had a lower significant difference than ≥1 ETRANK analysis; LOCF (66.7%) comparisons had a lower significant difference than MMRM.

Venlafaxine remission rates were significantly different from placebo in Glimmix analyses (38.9%) and LOCF_Logistic Regression comparisons (33.3%). Glimmix analyses (16.7%) revealed significant differences when LOCF_Logistic Regression did not, while LOCF_Logistic Regression (11.1%) revealed a difference when Glimmix did not. **Conclusions:** ETRANK demonstrated advantages in signal detection compared with MMRM. MMRM had no advantage over LOCF in detecting drug-placebo differences. No signal detection advantage was found for the Glimmix MMRM method versus LOCF_Logistic Regression analyses of remission rates.

References:

1. Mallinckrodt CH, Kaiser CJ, Watkin JG, Molenberghs G, Carroll RJ: The effect of correlation structure on treatment contrasts estimated from incomplete clinical trial data with likelihood-based repeated measures compared with last observation carri.
2. Entsuah R: ETRANK. a ranking procedure for handling missing data in clinical trials: application to venlafaxine extended-release depression clinical trial. J Biopharm Stat 1996; 6:457-475.

NR499 Tuesday, May 23, 3:00 PM - 5:00 PM

Safety and Effectiveness of OROS-Methylphenidate in Adults With Attention Deficit Hyperactivity Disorder (ADHD): Results of an Open Label Study

Angelo Fallu, M.D. *Clinique Woodward, 685 Woodward Street, Sherbrooke, PQ, J1G 1W4, Canada*, Rosanna Prinzo, Carin Binder

Educational Objectives:

At the conclusion of this presentation, the participant should be able :

1) to recognize that OROS*Methylphenidate is a safe and effective treatment option for adults with Attention Deficit Hyperactivity Disorder.

2) to recognize the benefit of long acting stimulants in the adult ADHD population

Summary:

Purpose: To evaluate the safety and effectiveness of OROS*-Methylphenidate for the treatment of adults with ADHD(ADHD).

Method: 30 patients 18-65 years, inclusive, with DSM-IV diagnosis of ADHD confirmed via clinical interview and the Wender Utah Rating Scale(WURS), with baseline investigator-rated CAARS ≥24, baseline CGI-S≥ 4 (at least "moderate" illness) and baseline MADRS ≤ 16 are being recruited into this 5 week study. Patients were started on 18mg OROS*-Methylphenidate for 3 days and titrated up, based on physician discretion and patient tolerability/effect to 36mg at Day 4 and then 54 or 72mg (2x36mg), if applicable, in 7 day increments. In the latter 2 weeks of the trial, the subject is expected to stay on the optimal dose achieved during the first 3 weeks. No other treatments for ADHD are permitted other than the study medication, OROS*-Methylphenidate. No new behavioural modification programs could be initiated while the patient was on study. Safety measures collected included physical examination, ECGs, vital sign and adverse event monitoring.

Results: N=26/30. Mean age=36.5+/-10.5 years. Mean OROS*-Methylphenidate dose was =51.2 +/- 14.1 mg with a mean treatment duration of 36.3 +/- 5.7 days. Mean baseline investigator-rated CAARS score=32.5+/-6.0 with a mean endpoint improvement = -18.7+/-9.8. (p<0.0001). Mean baseline CAARS self report total score=44.7 +/-10.3 with a mean improvement observed at endpoint = -20.0+/-15.8. (p<0.0001). Mean endpoint CGI-S change= -2.6+/-1.3 and 77% of patients were "completely" or "somewhat satisfied" with treatment at endpoint. The most frequent AEs reported were headache (62%) and decreased appetite (38%). Interim results are presented here but all results will be presented in the poster.

Conclusion: OROS*Methylphenidate may offer a safe and effective treatment option for adults suffering from ADHD.

References:

1. Adler LA, Chua HC. Management of ADHD in adults. J Clin Psychiatry 2002;63(Suppl 12):29-35.
2. Adler L, Cohen J. Diagnosis and evaluation of adults with attention-deficit/hyperactivity disorder. Psychiatr Clin North Am 2004;27(2):187-201.

NR500 Tuesday, May 23, 3:00 PM - 5:00 PM

Executive Functioning in Adult Attention Deficit Hyperactivity Disorder: Results of an Open Label Study Evaluating OROS-Methylphenidate

Angelo Fallu, M.D. *Clinique Woodward, 685 Woodward Street, Sherbrooke, PQ, J1G 1W4, Canada*, Caroline Richard, M.Psy., Rosanna Prinzo, Carin Binder

Educational Objectives:

At the conclusion of this presentation, the participant should be able :

1) To recognize the potential usefulness of long acting stimulants in ameliorating executive functioning in ADHD patients

2) to recognize that OROS*Methylphenidate is a safe treatment option for adults with Attention Deficit Hyperactivity Disorder.

3) to recognize the benefit of long acting stimulants in the adult ADHD population

Summary:

Purpose: To evaluate the safety of OROS*-Methylphenidate and its effect on executive functioning in adults with ADHD(ADHD).

Method: 30 patients 18-65 years, with DSM-IV diagnosis of ADHD confirmed via clinical interview and the Wender Utah Rating Scale(WURS), with baseline investigator-rated CAARS ≥24, baseline CGI-S≥4 (at least "moderate" illness) and baseline MADRS≤16 are being recruited into this 5 week study. Patients were started on 18mg OROS*Methylphenidate for 3 days and titrated up, based on physician discretion and patient tolerability/effect to 36mg at Day 4 and then 54 or 72mg (2x36mg), if applicable, in 7 day increments. In the latter 2 weeks of the trial, the subject is expected to stay on the optimal dose achieved during the first 3 weeks. No other treatments for ADHD are permitted other than the study medication. No new behavioural modification programs could be initiated while the patient was on study. Safety measures collected included physical examination, ECGs, vital sign and adverse event monitoring. Executive functioning measures collected included the Stroop Colour-Word test, COWAT verbal/category fluency test and the Working Memory Index of the WAIS-III.

Results: N=24/30. Mean age=36.5+/-10.5 years. Mean OROS*-Methylphenidate dose was =51.2 +/- 14.1 mg with a mean treatment duration=36.3 +/- 5.7 days. Mean baseline Stroop Colour-Word T-score=43.3+/-9.5 with a mean endpoint improvement = 6.7 +/-8.1(p=0.0005). Mean endpoint improvement in COWAT

Letter T-score= 5.3+/-5.4(p<0.0001). Mean endpoint improvement in COWAT Category T-score=5.0+/-7.7(p=0.005). Mean endpoint improvement in Working Memory Index percentile=13.5+/-15.1(p= 0.0002). The most frequent AEs reported were headache (62%) and decreased appetite (38%). Interim results are presented here but all results will be presented in the poster.

Conclusion: OROS*Methylphenidate may offer a safe treatment option for adults suffering from ADHD, with the added benefit of improving patients' executive functioning such as inhibition, verbal fluency and working memory.

References:

1. Barkley RA. Major life activity and health outcomes associated with attention-deficit/hyperactivity disorder. J Clin Psychiatry 2002;63(Suppl 12):10-5.
2. Lamberg L. ADHD often undiagnosed in adults: appropriate treatment may benefit work, family, social life. JAMA 2003;290;1565-7.

NR501 Tuesday, May 23, 3:00 PM - 5:00 PM

Ramifications of Switching Antipsychotics in the Treatment of Schizophrenia

Douglas E. Faries *Eli Lilly, Lilly Corporate Center, Indianapolis, IN, 46285*, Haya Ascher-Svanum, Allen W. Nyhuis, Bruce J. Kinon

Educational Objectives:

At the conclusion of this presentation, the participant should recognize that switching antipsychotics is an effective "rescue" option, but it is also costly in personal and economic terms. The optimal treatment strategy is to begin treatment with the antipsychotic most likely to lead to effective treatment for each individual patient.

Summary:

Objectives: To assess the clinical, functional, and economic ramifications of switching antipsychotics for any cause during treatment of schizophrenia.

Method: We used outpatient data from a randomized, open-label, 1-year cost-effectiveness trial of olanzapine, risperidone, and typical antipsychotics in the treatment of schizophrenia. Study protocol permitted switching of antipsychotics when clinically warranted. Resource utilization was abstracted from medical records. Treatment outcomes were assessed with standard psychiatric measures. Changes from pre-to-post switch were assessed among patients who switched from randomized antipsychotics. Switchers and non-switchers were compared on risk for crisis-related events (e.g., hospitalization).

Results: About one-third of the patients (30.2%, 185/612) were switched from randomized antipsychotics: 14.9% from olanzapine, 27.9% from risperidone, and 48.5% from typical antipsychotics. Following antipsychotic switch, switchers experienced significant improvements in symptoms and social relations (p<.001), and numerical cost reductions ($3.72 per day less, p=.320). Compared to non-switchers, switchers were at significantly higher risk for crisis-related events (p=.006), experienced them sooner (p=.004), and accrued higher crisis-related service costs (p<.05).**Conclusions**: Although switching antipsychotics is an effective "rescue" option, it is costly in personal and economic terms. The optimal treatment strategy is to begin treatment with the antipsychotic most likely to lead to effective treatment for each individual patient.

References:

1. Tunis SL, Kinon BJ, Faries DE, Ascher-Svanum H, Nyhuis AW, Aquila R. Cost-Effectiveness of Olanzapine as First-Line Treatment for Schizophrenia: Results From a Randomized, Open-Label, One-Year Trial. Value in Health, in press.
2. Hugenholtz GW, Heerdink ER, Nolen WA, et al. Less medication switching after initial start with atypical antipsychotics. European Journal of Neuropsychopharmacology 2002;14:1-5.

NR502 Tuesday, May 23, 3:00 PM - 5:00 PM

Cost and Effectiveness of Switching From Risperidone to Olanzapine in the Treatment of Schizophrenia

Douglas E. Faries *Eli Lilly and Company, US Commercial Info Sciences, Lilly Corporate Center, DC 5024, Indianapolis, IN, 46285*, Haya Ascher-Svanum, Bruce J. Kinon, Allen W. Nyhuis

Educational Objectives:

At the conclusion of this presentation, the participant should recognize that during the long-term treatment of patients with schizophrenia, switching from risperidone to olanzapine, when clinically warranted, appears to be a cost effective "rescue" option.

Summary:

Objectives: To assess changes in cost and effectiveness parameters following switch from risperidone to olanzapine during the long-term treatment of schizophrenia patients.

Methods: Patients were participants in a randomized, open-label, 1-year cost-effectiveness trial of olanzapine, risperidone, and typical antipsychotics in the treatment of schizophrenia. Study protocol permitted antipsychotic switching when clinically warranted. Resource utilization was systematically abstracted from medical records. Treatment outcomes were assessed with standard psychiatric measures. Statistical analyses assessed changes from pre-to-post switch among patients who were randomized to risperidone, but later switched to olanzapine for any cause.

Results: Sixty of the 218 (27.5%) patients randomized to risperidone switched antipsychotics - with 43 (72%) switching to olanzapine. Average duration on risperidone before switching to olanzapine was 86.1 days (mean maximum dose 4.5 mg/day). Most of these switchers (86%) completed the 1-year study on olanzapine (average maximum dose 13.3 mg/day). Following switch to olanzapine, patients experienced significant improvements on clinical and social parameters (both, p<.001), with 35.7% of the prior non-remitters achieving remission status. Mean total daily costs changed from $49.5/day pre-switch, to $44.4/day post-switch (non-significant difference).**Conclusions**: Olanzapine appears to be a cost effective "rescue" option for patients who require switching from risperidone in the long-term treatment of schizophrenia.

References:

1. Tunis SL, Kinon BJ, Faries DE, Ascher-Svanum H, Nyhuis AW, Aquila R. Cost-Effectiveness of Olanzapine as First-Line Treatment for Schizophrenia: Results From a Randomized, Open-Label, One-Year Trial. Value in Health, in press.
2. Hargreaves WA, Gibson PJ. Effectiveness and cost of risperidone and olanzapine for schizophrenia: a systematic review. CNS Drugs 2005;19:393-410.

NR503 Tuesday, May 23, 3:00 PM - 5:00 PM

Selegiline Transdermal System for the Treatment of Major Depressive Disorder: An Eight-Week, Double-Blind, Placebo-Controlled, Flexible-Dose Titration Trial

Alan D. Feiger, M.D. *Feiger Health Research Center, 3555 Lutheran Parkway #320, Wheat Ridge, CO, 80033-6021*, Karl Rickels, M.D., Moira A. Rynn, M.D., Daniel L. Zimbroff, M.D.

Educational Objectives:

At the conclusion of this presentation, participants should be able to:

1. Describe the results of an 8-week, double blind, placebo-controlled, flexible-dose titration trial of selegiline transdermal system for the treatment of depression.

2. Demonstrate an understanding of the ways in which selegiline transdermal system offers a new MAOI antidepressent option with an improved margin of safety.

Summary:

Introduction: The selegiline transdermal system (STS) is a MAO inhibitor (MAOI) with unique pharmacokinetic and pharmacodynamic properties. STS provides concentrations of selegiline necessary for antidepressant activity with reduced impact on the gastrointestinal MAO system.[1,2]

Objective: This study investigated the efficacy, safety, and tolerability of STS 6mg24hr to 12mg/24hr, in patients with MDD.

Method: Patients with MDD (N=265) were randomly assigned in a blinded fashion to receive treatment with either STS or a matching placebo patch for 8 weeks. Patients failing to meet or maintain response criteria at predetermined time points were titrated from 6mg/24hr to 9mg/24hr or 9mg/24hr to 12mg/24hr STS or placebo. Efficacy, safety, and tolerability were assessed at weeks 1, 2, 3, 5, and 8. A tyramine-restricted diet was not imposed.

Results: STS treatment resulted in significantly greater improvement ($P<0.05$) compared with placebo treatment on primary (HAM-D 28) and secondary (HAM-D 6-item Bech Subscale, HAM-D Item-1, MADRS, IDS-SR, and CGI-C) efficacy measures at 8 weeks. Treatment with STS was well tolerated, with the most frequent adverse events being application site reactions and insomnia. No clinically meaningful trends were apparent for clinical laboratory, vital signs, physical examination, or ECG results. No hypertensive crises were observed, and the occurrence of blood pressure elevation and orthostatic hypotension was comparable between STS and placebo.

Conclusion: Results from this multicenter, randomized, double-blind, placebo-controlled, flexible-dose trial provide further evidence of the efficacy of STS in the treatment of MDD. Additionally, this 8-week study demonstrates the short-term safety and tolerability of STS at doses of up to 12mg/24hr. Thus, STS may offer a new MAOI antidepressant option with an improved margin of safety.

References:

1. Gordon MN, Muller CD, Sherman KA, Morgan DG, Azzaro AJ, Wecker L: Oral versus transdermal selegiline: antidepressant-like activity in rats. Pharmacol Biochem Behav 1999;63:501-506.

2. Mawhinney M, Cole D, Azzaro AJ: Daily transdermal administration of selegiline to guinea-pigs preferentially inhibits monoamine oxidase activity in brain when compared with intestinal and hepatic tissues. J Pharmacy Pharmacol 2003;55:27-34.

NR504 Tuesday, May 23, 3:00 PM - 5:00 PM

Escitalopram in Relapse Prevention in Patients With OCD

Naomi Fineberg, Ph.D. *Queen Elizabeth II Hospital, Howlands, Welnyn Garden City, AL7 4HQ, United Kingdom*, Ole Lemming, Brigitte Tonnior

Educational Objectives:

The participant will obtain knowledge concerning the prevention of relapse in patients with obsessive-compulsive disorder using escitalopram treatment.

Summary:

Introduction: OCD is a common chronic disorder with a lifetime prevalence of 1-4% (1). Comorbid disorders such as anxiety and depression can complicate the initial diagnosis of OCD as well as response and relapse rates in studies (2). The primary objective of this study was to compare the efficacy of escitalopram 10 or 20mg/day with that of placebo in preventing relapse during 24 weeks in outpatients with OCD who had responded to 16 weeks open-label treatment with escitalopram.

Methods: This was a multinational, randomised, double blind, placebo-controlled, flexible to fixed dose relapse prevention study with escitalopram in outpatients with OCD. Cases with relevant comorbidity, including coexisting depression and anxiety, were excluded. The study consisted of two periods: a 16-week open-label period with 10-20mg escitalopram followed by a 24-week double blind, placebo-controlled period, and a 1-week taper period. Patients who had responded to treatment (≥25% decrease in their Yale-Brown Obsessive Compulsive Scale total score) by the end of the 16-week open-label period were eligible for randomisation to either escitalopram (10 or 20mg/day) or placebo.

Results: Of 472 patients treated in the open-label period, 320 were randomised to treatment with escitalopram (n=163) or placebo (n=157). The primary analysis showed a clear beneficial effect of escitalopram relative to placebo on the time to relapse (log-rank test, $p<0.001$). The risk of relapse was 2.7 times higher for placebo- than for escitalopram-treated patients (chi-square test, $p<0.001$). Significantly fewer escitalopram-treated patients relapsed (23%) compared with placebo (52%) (chi-square test, $p<0.001$). Escitalopram was well tolerated; 4 escitalopram-treated patients and 4 placebo-treated patients were withdrawn due to adverse events during double-blind treatment (NS). The overall withdrawal rate, excluding relapses, was 9.6% for escitalopram and 9.4% for placebo during the double-blind period (NS).

Conclusion: Escitalopram was effective in preventing relapse of OCD and was well tolerated as continuation treatment.

References:

1. Hollander R, Greenwald S, Neville, et al. Uncomplicated and comorbid obsessive-compulsive disorder in an epidemiologic sample. Depress Anxiety 1997; 4: 111-119.

2. Hollander E, Allen A, Steiner M, Wheadon DE, Oakes R, Burnham DB; Paroxetine OCD Study Group. Acute and long-term treatment and prevention of relapse of obsessive-compulsive disorder with paroxetine. J Clin Psychiatry. 2003;64:1113-21.

NR505 Tuesday, May 23, 3:00 PM - 5:00 PM

Antipsychotics and Diabetes Mellitus Among Schizophrenic Patients: Analysis of the National Health Insurance Database in Taiwan

Susan Shur-Fen Gau, M.D. *National Taiwan University Hospital, Department of Psychiatry, No. 7, Chung-Shan South Rd, Taipei, Taiwan Republic of China*, Churn-Shiouh Gau, Ph.D., Ching-Jui Chang, M.D., Hung-Chun Lai, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that atypical antipsychotics may not increase higher risk for Diabetes Mellitus than typical antipsychotics in Taiwan.

Summary:

Objectives: Western literature has documented an increased risk for diabetes mellitus (DM) among schizophrenic patients (SP), particularly for those patients treated with atypical antipsychotics. The objectives of this study are to obtain the prevalence and incidence of DM among schizophrenic inpatients from 1997 to 2003 and to compare the exposures of antipsychotics and other DM-related medications between patients with incident DM and the controls from 2001 to 2003.

Methods: The National Health Insurance Research Database - Psychiatric Inpatient Medical Claim Dataset (PIMC2002) was

used. A nested matched case-control study design was used to include 2631 SP with incident DM in 2001, 2002, and 2003; and 10, 524 SP without any diagnosis of DM from 1996 to 2003. The exposures included comorbid disorders, medications reported to related to risk for DM, antipsychotics before the first diagnosis of DM. Conditional logistic regression model was used for matched case-control analysis.

Results: The prevalence of DM in SP from 1997 (9.7%) to 2003 (16.5%) were higher than that of general population in Taiwan (2.0%). The incidence rates of DM were around 4 per 100 person-year. SP with DM were more likely to have comorbid disorders of affective disorder, hyperlipidemia, hypertension, obesity diagnosis, ischemic heart disease, heart failure, and alcoholism; and exposures to systemic steroid, oral contraceptives, thiazide, phenytoin, valproic acid, beta-blocker, alpha-blocker, risperidone, olanzapine, and quetiapine. The effect of the three atypical antipsychotics on risk for DM among SP was small but significant (odds ratios ranging from 1.05 to 1.12); however, the significant effects disappeared when controlling for comorbid disorders or other medication.

Conclusions: This study using a national sample did not support a differential risk for DM between SP treated with typical and atypical; and among SP treated with typical antipsychotics, clozapine, olanzapine, risperidone, quetiapine, and zotepine.

References:

1. Holt RI, Peveler RC, Byrne CD: Schizophrenia, the metabolic syndrome and diabetes. Diabetic Medicine 2004; 21:515-23.
2. Bellantuono C, Tentoni L, Donda P: Antipsychotic drugs and risk of type 2 diabetes: an evidence-based approach. Human Psychopharmacology 2004; 19:549-58.

NR506 Tuesday, May 23, 3:00 PM - 5:00 PM

A Meta-Analysis of Pharmacological Interventions in Management of SSRI-Induced Sexual Dysfunction

Ellen Haller, M.D. *University of California San Francisco, Box F-0984/401 Parnassus Avenue, San Francisco, CA, 94143-0984*, Bahar Ghahremani, B.A., Brian Jersky, Ph.D.

Educational Objectives:

At the conclusion of this session, the participants should be able to identify the pharmacological interventions studied up to now and use the findings of this review to help guide the management of patients suffering from SSRI-induced sexual dysfunction.

Summary:

Objectives

The primary purpose of this review was to assess and compare the efficacy of pharmacological interventions in management of SSRI-induced sexual dysfunction.

Method

We searched the CENTRAL database (Cochrane Library issue 4, 2005), PubMed (January 1966 - July 2005), and the references of the identified studies. Randomized Controlled Trials (RCTs) were selected and screened for inclusion criteria. Eleven trials involving 705 participants met inclsions criteria. The primary reviewer performed data collection and quality assessment of these 11 studies.

Main results

Data were analyzed using the Review Manager software (version 4.2). Standardized Mean Difference (SMD) was calculated as the summary statistic for each intervention. The data collected were pooled using the random effect method of analysis, and a pooled treatment effect was calculated. Our pooled analysis failed to show any statistically significant difference between the following augmentation therapies and placebo: buspirone [p=0.94, SMD=0.10], Ginkgo biloba [p=0.96, SMD=0.07], granisetron [p=0.93, SMD=0.13], or sildenafil [p=0.92, SMD=-0.13]. Individual trials of additional interventions also failed to show a beneficial effect on the pre-specified outcome: amantadine (p=0.70, SMD=0.77), bupropion Sustained Release (p=0.80, SMD=0.5), ephedrine (p=0.95, SMD=-0.12), mirtazapine (p=0.98, SMD=0.05), olanzapine (p=0.94, SMD=0.14), or yohimbine (p=0.90, SMD=0.25).

Conclusions

The clinical application of these therapies is not supported by the published research studies to date. Future adequately powered RCTs on these augmentation therapies should implement rigorous methods to maximize internal validity. Standardized rating scales of sexual functioning need to be consistently used both at baseline and to measure response to interventions. SSRIs are very widely prescribed to treat both depression and anxiety disorders but commonly cause sexual side effects leading to lack of treatment adherence. Due to this serious problem, more research into ways of minimizing sexual dysfunction is critically important.

References:

1. Higgins JPT, Green S, editors: Cochrane Handbook for Systematic Reviews of Interventions 4.2.4 [updated March 2005]. Chichester, UK: John Wiley & Sons, Ltd., 2005.
2. Montejo AL, Llorca G, Izquierdo JA, Rico-Villademoros F: Incidence of Sexual Dysfunction Associated With Antidepressant Agents: A Prospective Multicenter Study of 1022 Outpatients. J Clin Psychiatry 2001; 62(suppl 3):10-21.

NR507 Tuesday, May 23, 3:00 PM - 5:00 PM

Spatiotemporal Pattern Analysis of EEGs of Alexithymic Individuals

Byung-Joo Ham, Prof. Dr. *Hangang Sacred Heart Hospital, Hallym University Medical School, Psychiatry, 94-200 Youngdungpo-Dong, Youngdungpo-Gu, Seoul, 150-719, Republic of Korea*, Sung-Gon Ryu, Prof. Dr., Dong-Woo Lee, Prof. Dr., Seung-Ho Ryu, Kang-Seob Oh, Prof. Dr., Han Yong Jung, Prof. Dr., Ihn-Geun Choi, Prof. Dr.

Educational Objectives:

The aim of the presentation is to assess whether the differences of EEGs exist between alexithymics and non-alexithymics during resting condition. At the conclusion of this presentation, the participant should be able to recognize the neurobiology of alxexithymia.

Summary:

The aim of the present study is to assess whether the differences of EEGs exist between alexithymics and non-alexithymics during resting condition. In order to perform such an analysis and investigate the dynamic behavior of a brain, we have examined the spatiotemporal behavior of EEG recorded from alexithymics and non-alexithymics. EEG signals recorded from 16 electrodes in 13 alexithymics and 13 age/sex-matched non-alexithymics. We estimated the spatiotemporal pattern of the EEG recordings by using KL decomposition method. As a result, non-alexithymics and alexithymics exhibited similar primary patterns. However, the secondary patterns of alexithymics differed from those of nonalexithymics at F7, F8, and T3 channels, with the definitely opposite polarity at the right and left hemispheres when compared with non-alexithymics. These all findings support the neurological models, i.e. the dysfunction of the right hemisphere and deficiency in the frontal lobe area, for alexithymia generally adopted, and provide the first EEG evidence by means of the spatiotemporal EEG patterns during resting condition.

References:

1. Lane RD, Ahern GL, Schwartz GE, Kaszniak AW. Is alexithymia the emotional equivalent of blindsight?. Biological Psychiatry 1997;42: 834-844.

2. Taylor GJ. Recent developments in alexuthymia theory and research. Canadian Journal of Psychiatry 2000;45:134-142.

NR508 Tuesday, May 23, 3:00 PM - 5:00 PM

EEG With Electrical Tomography (LORETA) of OCD During Paroxetine Withdrawal Shows Temporal and Parietal Lobe Dysfunctions

Cary L. Hamlin, M.D. *Atlantic Healthcare System, Psychiatry, 385-2B Route 24, Chester, NJ, 07930*

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the symptoms of SSRI withdrawal syndrome, know that paroxetine can cause it, know that it occurs in OCD patients, and know that it can be associated with EEG abnormalities in the anterior temporal lobe, know that OCD patients can have repeatable abnormalities in the insula, archiocingulate gyrus, and supplemental motor cortex that are demonstrable using EEG LORETA.

Summary:

SSRI discontinuation syndrome symptoms, dizziness, shock-like sensations, nausea, diarrhea, gait disturbances, visual disturbances, tremor, and fatigue, begin from 1 to 7 days after lowering an SSRI during treatment. Paroxetine is the prototypical SSRI to cause discontinuation syndrome, and it has been reported in OCD patients withdrawing from paroxetine. Research here describes the changes in EEG tomography that accompanied SSRI discontinuation syndrome, from paroxetine withdrawal, in a 63 yr old male OCD (DSM-IV) patient. While tapering off months of paroxetine 60 mg qd, he had the new onset of shock-like sensations, dizziness, visual disturbances, and nausea, exacerbated by eye blinking. A 32 lead extended International 10/20 montage EEG was digitalized at 512 samples sec^-1 using a BioSemi amplifier-A/D converter. LORETA processing of the EEG data produces a mapping of spectral analysis data upon cortical regions of an averaged Talairach MRI Atlas. The patient's electrical tomogram was remapped against an EEG database of task, handedness, age, and gender matched neurometric normal controls. The resultant z-scores were compared by paired-"t" test to those he had previously obtained, while taking paroxetine before SSRI discontinuation symptoms began. Laplacian transformation of his routine EEG revealed frequent single spikes (300 uA) in lead T7, and a few 6 spike trains which followed eye blinks. Mu (12-15 Hz) power was abnormally decreased in the left anterior temporal lobe (Brod38), and this was significantly different from before withdrawal. Delta (1-3 Hz) power was abnormally increased in the supplemental sensory cortex (medial Brod07) bilaterally only during withdrawal. Unchanged in both EEGs, (19-30 Hz) Beta power was abnormally increased in the insula, archiocingulate gyrus, and supplemental motor cortex bilaterally. Mu power was abnormally increased in the insula, archiocingulate gyrus, and supplemental motor cortex bilaterally, ie. where Beta power was consistently elevated, while taking paroxetine, but not so during paroxetine withdrawal.

References:

1. Keuthen NJ, Cyr P, Ricciardi JA, Minichiello WE, Buttolph ML, Jenike MA. : Medication withdrawal symptoms in obsessive-compulsive disorder patients treated with paroxetine. J Clin Psychopharmacol. 1994 Jun;14(3):206-7.

2. Thatcher, R., Biver, C., North, D. : Evaluation and Validity of a LORETA Normative EEG Database. Clin EEG Neurosci. 2005 Apr;36(2):116-22.

NR509 Tuesday, May 23, 3:00 PM - 5:00 PM

The Relationship Between Beck Depression Inventory (BDI) Score and Heart Rate Variability (HRV) in General Population

Chang Woo Han *Hanyang University Hospital, Psychiatry, Psychiatry, Hanyang Univ Hospital, Haengdang-Dong, Sungdong-Ku, Seoul, 133-792, Republic of Korea*, Seok Hyeon Kim, Yang Suk Kim, Jung Woo Ahn, Hwallip Bae

Educational Objectives:

At the conclusion of this presentation, the participitant should be able to recognize that depressive symptom seems to influence autonomic neurocardiac regulation between the sympathetic and parasympathetic system even in the population without diagnosis of depressive disorder.

Summary:

Objectives: Heart Rate Variability (HRV) refers to the degree of fluctuations in the length of the intervals between heart beats. The analysis of HRV is regarded as a reliable non-invasive test for quantitative assessment of cardiovascular autonomic regulations. Depression is known to be associated with an increased risk of cardiovascular mortality, due to the reduction of vagal activity to the heart. In the previous reports, HRV has been shown to be reduced in patient with depressive disorder. This study is designed to examine the relationship between depressive symptoms measured by self-reporting depression scale and HRV in general population without history of depressive disorder.

Methods: 298 subjects were recruited from an annual health survey in a suburbs of Korea. The history of any psychiatric disorder was asked before recruitment. They fasted over the previous night and did not drink any caffeinated beverage and smoke. After 20 minute rest in the examination room, the time and frequency domain HRV indices(5-min resting study) were examined and standardized quantitatively. After HRV test, they completed the Beck Depression Inventory (BDI) in a private room..

Results: 142 subjects were excluded by the ECG result. HRV and BDI score of 156 subjects were analyzed. The HRV was shown to be negatively correlated with BDI score. Low frequency(LF:0.04-0.15 Hz), high frequency(HF: 0.15-0.4 Hz) were significantly lowered reduced as BDI score(LF: r=-0213, p<0.01, HF: r=-0.193, p<0.05).

Conclusions: As in the previous studies with the patients with depressive disorder, HRV of the people with depressive symptoms in BDI significantly decreased. Depressive symptom seems to influence autonomic neurocardiac regulation between the sympathetic and parasympathetic system even in the population without diagnosis of depressive disorder.

References:

1. Cohen, H., Analysis of heart rate variability in posttraumatic stress disorder patients in response to a trauma-related reminder. Biological Psychiatry 1998, 44; 1054-1059.

2. Cohen, H., Power spectral analysis of heart rate variability in posttraumatic stress disorder patients. Biological Psychiatry 1997, 41; 627-629.

NR510 Tuesday, May 23, 3:00 PM - 5:00 PM

Satisfaction With Long-Acting, Injectable Risperidone

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Educational Objectives:

To evaluate the satisfaction level of the patients and their caregivers to the long-acting injectable risperidone as a customer.

Summary:

Background: The satisfaction of treatments received by schizophrenia patients can strongly influence the treatment adherence and long-term outcome. Atypical antispychotics reportedly have better adherence rates owing to a lower incidence of side effects and especially higher levels of patient satisfaction and acceptability. However, the satisfaction with long-acting injectable atypical antipsychotics has not been compared with that of oral atypical antipsychotics. The objective of the study was to elucidate any differences in patient and caregiver satisfaction between long-acting injectable risperidone and oral atypical antipsychotics. *Methods:* Forty-seven patients with schizophrenia who were receiving treatment with long-acting injectable risperidone and their caregivers were surveyed using a semi-structured questionnaire about their satisfaction with the drug and its acceptability. Sixty-two patients currently taking oral atypical antipsychotics - and their caregivers - were also surveyed for comparison. In the questionnaire, subjects were asked to mark their satisfaction level on a 10-point visual analogue scale (VAS). Items to elucidate discomfort and side effects experienced were also included. *Results:* The VAS satisfaction score was significantly higher for patients receiving long-acting injectable risperidone than for those taking oral atypical antipsychotics (7.53 versus 6.87, $p < 0.05$). The overall VAS score was significantly higher for caregivers of both groups of patients than for the patients themselves (8.04 versus 7.16, $p < 0.000$). *Conclusion:* A new drug delivery system - long-acting injectable risperidone - may offer better adherence in schizophrenia treatment, owing to higher levels of patient and caregiver satisfaction, and thereby result in improved treatment outcomes.

References:

1. Csernansky JG, Mahmoud R, Brenner R; A comparison of risperidone and haloperidol for the prevention of relapse in patients with schizophrenia. N Engl J Med 2002;346:16-22.
2. Kalali A; Patient satisfaction with and acceptability of atypical antipsychotics. Curr Med Res Opin 1999;15:135-7.

NR511 Tuesday, May 23, 3:00 PM - 5:00 PM

Genetic Factor of Alcohol Metabolism Might Protect Early Onset Alcohol Dependence

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Educational Objectives:

We aimed to find genetic factor which is related to early onset of alcohol consumptions in alcohol dependence. It would be helpful for the understanding of early onset alcohol abusers in biology. Biological understanding of early onset alcohol abuse could decrease the number of chronic alcohol dependence and help to invent new treatment drugs for alcohol dependence

Summary:

Introduction

The biological etiology of early onset alcohol dependence derived from different theories such as craving, withdrawal symptoms, primary psychiatric disorder, and the metabolism of alcohol itself.

Method

The patients were classified into early onset alcohol dependence group (OAD) (before age 18yrs) and late onset alcohol dependence group (LAD) (after age 19yrs).

We investigated DRD2, DRD4, Gamma-aminobutyric acid A alpha 6 and NRH-quinone oxidoreductase 2 (NQO2) regulation gene polymorphism in 108 alcohol dependence patients

Addiction severity index (ASI) and Beck depression Inventory (BDI) were applied for clinical symptom evaluation. Neurocognitive functions were checked by Trail making test A/B, Stroop color-world test, and Wisconsin card sorting test.

Result

The number of OAD group and LAD was 80 and 136, respectively. There was only significant difference between OAD and LAD in NQO2 gene distribution. The number of D carrier gene of NQO2 in OAD was lower than that of LAD. D allele was negatively correlated with ASI scores. There were no significant differences between OAD and LAD in neurocognitive tests and clinical scales.

Discussion

NRH-quinone oxidoreductase 2 (NQO2) is regarded as important factors for detoxification of alcohol in the CNS. D allele of NQO2 was associated with alcohol withdrawal symptoms. Innate alcohol metabolic efficacy would play important role in the pathogenesis of early onset alcohol dependence.

References:

1. Okubo T, Harada S, Higuchi S, Matsushita S. Association analyses between polymorphisms of the phase II detoxification enzymes (GSTM1, NQO1, NQO2) and alcohol withdrawal symptoms. Alcohol Clin Exp Res 2003; 27(8 Suppl):68S-71S.
2. Hertling I, Ramskogler K, Riegler A, Walter H, Mader R, Lesch OM. Craving for alcohol and prevention of relapse. Wien Klin Wochenschr 2001; Oct; 15;113:717-26.

NR512 Tuesday, May 23, 3:00 PM - 5:00 PM

Weight and Body-Mass Index in Patients Receiving Open-Label Lamotrigine With or Without Concomitant Valproate, Antipsychotics, or Antidepressants

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Educational Objectives:

At the conclusion of this presentation, the participant should be able understand patient response and tolerability to lamotrigine treatment.

Summary:

Objective: The current analysis evaluated changes in weight and body-mass index (BMI) in patients treated with lamotrigine in the presence and absence of concomitant valproate or antipsychotics.

Methods: A post hoc analysis was conducted from a prospective, open-label study of lamotrigine[1] in 1175 patients with bipolar I disorder designed to assess the rate of rash in patients with or without specific dermatological precautions. Lamotrigine was administered for 12 weeks, including a 5-week titration period (target dosage 200 mg/day). Weight and BMI was measured at baseline, week 5 and week 12 visits.

Results: Baseline weight was statistically significantly higher in patients taking concomitant valproate versus without (199.1 ± 49.07 versus 184.7 ± 47.53 lb, $P < 0.0001$) and was statistically significantly higher in patients taking concomitant antipsychotics versus without (192.7 ± 47.31 versus 186.1 ± 48.48 lb, $P < 0.05$). Statistically significant changes in weight were not observed between treatment groups. Weight changes from baseline to week

12 were -0.2 ± 6.82 lb with valproate, 0.0 ± 8.40 lb without valproate, -0.4 ± 7.99 lb with antipsychotics, and 0.0 ± 8.14 lb without antipsychotics ($P>0.05$ for all group comparisons). Statistically significant changes in BMI were not observed between treatment groups. BMI changes from baseline to week 12 were 0.0 ± 1.07 with valproate, 0.0 ± 1.41 without valproate, -0.1 ± 1.34 with antipsychotics, and 0.0 ± 1.34 without antipsychotics ($P>0.05$).

Conclusion: These results are consistent with previous findings that lamotrigine is weight neutral in patients with bipolar disorder[2] and suggest that lamotrigine may be given to patients with concomitant medications that are frequently associated with increased body weight without causing additional weight gain.

References:

1. Ketter TA et al. The Effect of Dermatologic Precautions on the Incidence of Rash with Addition of Lamotrigine in the Treatment of Bipolar I Disorder. J Clin Psych. In Press.
2. Calabrese JR, Suppes T, Bowden CL, et al, for the Lamictal 614 Study Group. A double-blind, placebo-controlled, prophylaxis study of lamotrigine in rapid-cycling bipolar disorder. Lamictal 614 Study Group. J Clin Psychiatry. 2000;61:841-850.

NR513 Tuesday, May 23, 3:00 PM - 5:00 PM

Cerebral SPECT in Opiate Dependents With Dual Pathology

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Educational Objectives:

At the conclusion of this presentation the participants should know that neurobiology of substance use disorders and personality disorders has become an important branch of research works. A high rate of patients with a substance use disorder has also a personality disorder. The importance of dual pathology that can not be ignore by the research, trying to improve the treatments for these patients. Discovering the cerebral structures behind dual pathology, although is not an easy road, can lead to a better understanding of an important group of patients. New techniques in neuroimaging can be used to study how the brain activity can be altered by both pathologies. Establishing the cerebral structures and the relationships of both pathologies can improve the knowledge of futures psychiatrists and psychologists and be considered a new tool for better diagnosis and treatments.

Summary:

Almost all research works show hypoactivity in frontal and prefrontal lobes. The main hypoactive subcortical areas in BPD are: basal ganglions, caudate, lenticular nuclei and right side of nuclei ventral striate, thalamic area, limbic regions, specifically anterior cingulate, a region with many opiate receptors and could be related with pain experience and tendency to self mutilation (Juengling y cols, 2003).

SPECT studies suggest low activity in prefrontal, frontal, temporal and parietal cortex in opiate dependents. Two of them show hypoactivity asymmetry, with right cerebral areas less activated than left cerebral areas (Pezawas y cols, 2002).

Objectives: analyze cerebral structures in opiate dependence with a comorbid BPD, to study a possible causality in comorbid pathology analyzing the obtained images, to establish SPECT as a useful diagnosis technique to discriminate both single pathologies and comorbid pathology and to check sex differences. *Results:* sample of 12 probands (N=12). Group A (n=4): Opiate Dependents. Group B (n=4): Opiate Dependents with BPD as a comorbid pathology. Group C (n=4): Control. All probands were white Caucasian. Mean age was 33,75 years (SD=6,95). 58,3% were men and 41,7% women. Images in the 12 persons show significant statistical differences inter groups in frontal right lobe ($P<0.015$) and temporal right lobe ($P<0.036$). Ad-hoc measures reveal that the differences were between dual pathology group and control group. So, differences exist in frontal right lobe ($P<0.014$) and temporal right lobe ($P<0.037$) between dual pathology group and control group. A strong correlation was seen between frontal right lobe and temporal right lobe (0,916; $P<0,001$), what suggest a connection between both lobes in these patients. No sex differences were appreciated. *Conclusion:* Dual pathology group presents an accused decreased activity in frontal and temporal right cerebral areas. This frontal-temporal hypoactivity in right cerebral areas could be the addition of both disorders.

References:

1. Juengling FD, Schmahl C, Heblinger B, Ebert D, Bremner JD, Gostomzyk J et al: Positron emission tomography in female patients with borderline personality disorder. Journal of Psychiatric Research. 2003;37:109-15.
2. Pezawas L, Fischer G, Podreka I, Schindler S, Bruce T, Jagsch R et al: Opioid addiction changes cerebral flow symmetry. Neuropsychobiology 2002; 45(2):67-73.

NR514 Tuesday, May 23, 3:00 PM - 5:00 PM

Sustained Remission and Cognitive Improvements in Patients With Schizophrenia Switched to a New Atypical Antipsychotic

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Educational Objectives:

To increase understanding of the development of symptomatic remission in schizophrenia

To increase understanding of the relationship between cognitive improvement and development of remission in schizophrenia

This presentation will also evaluate the potential functional significance of development of symptomatic remission in the context of no change in cognitive functioning

Summary:

Background: A definition of remission in schizophrenia has been proposed. However, cognitive impairments are better predictors of functional outcomes than symptoms. We examined the development of remission and the association of neuropsychological improvements with remission in patients with schizophrenia whose medication was switched to a new atypical medication, ziprasidone. **Methods**: 184 patients were switched from previous treatment with risperidone, olanzapine, or conventional antipsychotics to open-label ziprasidone. We rated symptoms with the PANSS at baseline prior to the switch and after 6 weeks and 6 months of treatment. We also performed a neuropsychological assessment, which generated a composite score examined for improvements in the same time frame **Results**: Of the 184 pateints, 48 (26.1% of the total sample) met remission criteria at baseline. Of these cases, 41 (85%) sustained their remission to the endpoint.. Of the remaining 136 cases, 60 developed remission at the 6-month follow-up. Thus, a total of 101 of 184 cases (55%) were in remission at the endpoint. A comparable number of the patients, fifty nine (34%), improved by 0.5 SD or more in their cognitive performance. There were no baseline cognitive differences between patients who were and were not in remission and baseline cognitive performance did not predict remission. Further, achieving remission was not correlated with cognitive improvements. 33 patients achieved both clinical remission and 0.5 SD improvements in their cognitive performance. **Implications**: After a switch from previous treatment to open-label ziprasi-

done more than half of patients achieved remission over 6 months and 32% of patients achieving remission experienced concurrent cognitive improvement. Since cognitive performance at baseline and cognitive changes did not converge overall with development of remission, later research will be required to determine which aspects of improvement (clinical remission and/or cognitive improvements) predict functional improvements.

References:

1. Andreasen NC, Carpenter, WT, Kane JM, Lasser RA, Marder SR, Weinberger DR. Remission in schizophrenia: proposed criteria and rationale for consensus. Am J Psychiatr 2005, 162:441-449.
2. Lasser RA, Bossie CA, Gharabawai GM, Kane JM. Remission in schizophrenia: Results from a one-year study of injectable risperidone. Schizophr Res 2005; 77: 215-227.

NR515 Tuesday, May 23, 3:00 PM - 5:00 PM

Comparative Efficacy of Right Unilateral and Bilateral Electroconvulsive Therapy (ECT) and Augmentation With Antidepressants During Acute ECT

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Educational Objectives:

At the conclusion of this presentation the participant should be able to administer electroconvulsive therapy to treat patients with major depression using procedures that will optimize the efficacy and minimize the side effects of the treatment.

Summary:

Introduction: Questions persist about the optimally effective procedures for administering ECT in the treatment of depression. Two key issues are the relative efficacy of right unilateral (RUL) and bilateral (BL) ECT and the risks and benefits of pharmacological augmentation with antidepressants during acute ECT. In this report we provide data from a multi-site study of 295 patients with major depression that compared the efficacy of RUL and BL ECT and examined the effect of concurrent antidepressant administration during ECT.

Methods: On entry into the study, patients were randomized to two treatment conditions, high dose RUL ECT or low dose BL ECT and concurrent treatment with nortriptyline (NT), venlafaxine (VEN) or placebo, using a parallel group, double masked design stratified by resistance to antidepressant pharmacotherapy and the presence or absence of psychosis. Patients continued ECT until meeting remission criteria of 10 or less on the Hamilton Rating Scale for Depression following two successive ECT.

Results: There was no significant difference in the remission rates of patients receiving high dose RUL ECT or low dose BL ECT. Patients receiving treatment with NT or VEN during ECT had a 15% higher remission rate than patients receiving placebo and there was no significant difference between the antidepressants.

Conclusions: These results demonstrate that high dose RUL ECT and low dose BL ECT are of equivalent efficacy in the treatment of depression. In addition, augmenting acute ECT with concurrent antidepressant treatment provides a significant increase in efficacy compared to patients receiving ECT alone. The final analyses will be presented as well as a discussion of the differences between the randomized conditions.

References:

1. Sackeim HA, Prudic J, Devanand DP, Nobler MS, Lisanby SH, Peyser S, Linda Fitzsimons L, Moody BJ, Clark J: A Prospective, Randomized, Double-blind Comparison of Bilateral and Right Unilateral Electroconvulsive Therapy at Different Stimulus Intensitie.
2. Nelson JP, Benjamin L: Efficacy and safety of combined ECT and tricyclic antidepressant drugs in the treatment of depressed geriatric patients. Convulsive Ther 1989; 5:321-329.

NR516 Tuesday, May 23, 3:00 PM - 5:00 PM

Escitalopram for Bereavement-Related Depression

Paula L. Hensley, M.D. *University of New Mexico, Department of Psychiatry, 1 University of New Mexico, UNM Dept. of Psychiatry MSC 09 5030, Albuquerque, NM, 87131*, Carol K. Slonimski, Ph.D., Paula J. Clayton, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should recognize that escitalopram is effective in the treatment of bereavement-related major depressive disorder.

Summary:

Objective: To examine the efficacy of escitalopram in treating MDD associated with bereavement and grief symptoms.

Method: Thirty adults were treated with escitalopram in open fashion for a major depressive episode following loss of a close family member (parent, sibling, child, or spouse/significant other). The study period was twelve weeks. The maximum dose for the first four weeks was 10 mg per day and could be increased to 20 mg per day after four weeks. Efficacy assessments were the Clinical Global Impression (CGI) scales for depression and grief, Hamilton Depression Rating Scale (HAM-D), Hamilton Anxiety Rating Scale (HAM-A), Montgomery and Asberg Depression Rating Scale (MADRS), the Texas Revised Inventory of Grief (TRIG), and the Inventory of Complicated Grief (ICG).

Results: Twenty-nine of thirty participants returned for at least one set of efficacy measures after starting medication. Twenty-four of twenty-nine (82.8%) were treatment responders on the CGI for depression. Fourteen of twenty-nine (48.3%) were treatment responders on the CGI for grief symptoms. Escitalopram significantly reduced depressive symptoms (HAM-D, MADRS both $P < 0.001$) and anxiety (HAM-A, $P < 0.001$) over time. Escitalopram was well tolerated.

Conclusions: Escitalopram improved depressive, anxiety, and grief symptoms in individuals experiencing a major depressive episode related to the loss of a loved one.

References:

1. Zisook S, Shuchter SR, Pedrelli P, Sable J, Deaciuc SC: Bupropion sustained release for bereavement: results of an open trial. J Clin Psychiatry 2001; 62:4, 227-230.
2. Pasternak RE, Reynolds III CF, Schlernitzauer M, Hoch CC, Buysse DJ, Houck PR, Perel JM: Acute open-label trial of nortriptyline therapy of bereavement-related depression in late life. J Clin Psychiatry 1991; 52:7, 307-310.

NR517 Tuesday, May 23, 3:00 PM - 5:00 PM

Comparison of Weight Change on Divalproex DR and Divalproex ER

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Educational Objectives:

At the conclusion of this presentation the participant should be able to discuss the differential effects of Divalproex DR and Divalproex ER on weight changes during long term treatment.

Summary:

Introduction: In a previously reported study, 55 consecutive psychiatric patients were safely switched from Divalproex DR to an equal dose of Divalproex Extended Release with good tolerability. Changes in blood levels, adverse events, and psychiatric symptoms were reported. 37 of those 55 patients have been enrolled into an open-label, long-term extension of Divalproex Extended Release to assess weight change. Prior studies, including placebo controlled trials of Divalproex DR and Divalproex Extended Release, have shown a lower prevalence of weight gain with Divalproex Extended Release, but these were not head-to-head trials. **Methods:** In this study 37 patients on Divalproex Extended Release were followed after the switch for as long as they had been on Divalproex DR prior to the switch, to compare weight change in the same patients on both medications. **Results:** 37 patients were on Divalproex DR for an average of 377 days prior to the switch (median = 328). Their mean weight at baseline was 183.4 lbs, (BMI = 31.6). At the switch the mean weight was 190.1 lbs, (BMI = 32.7), an increase in mean weight of 6.7 lbs. At follow-up, an average of 383 days after the switch (median = 344), their weight was 188.1 lbs, a decrease in mean weight of -2.0 lbs. The difference between Divalproex DR and Extended Release mean weight change was significant. (p = .0056). 34 patients were on 1-3 concomitant medications. Only 10 of these patients had a change of concomitant medications during the study period. When these ten patients were excluded, the results in mean weight changes (+ 6.2 on Divalproex DR, -4.2 on Divalproex Extended Release) remained statistically significant (p = .0053) **Conclusion:** Divalproex Extended Release is preferable to Divalproex DR with regard to weight change over a one year period.

References:

1. Horne, R.L., Cunanan, C. Safety and Efficacy of Switching Psychiatric Patients from a Delayed-Release to an Extended-Release Formulation of Divalproex Sodium. J Clin . Psychopharmacol 2003, 23(2), 176-81.
2. Smith, M.C., Centorrino, F., Welge, J.A., Collins, M.A. Clinical Comparison of Extended-Release Divalproex versus Delayed-Release Divalproex: Pooled Data Analyses from Nine Trials. Epilepsy & Behavior 2004, 5, 746-51.

NR518 Tuesday, May 23, 3:00 PM - 5:00 PM

Concomitant Antidepressant Treatment During Acute Electroconvulsive Therapy (ECT): Side Effects?

Keith E. Isenberg, M.D. *Washington Univ Sch of Med, Psychiatry, 660 South Euclid Avenue, Campus Box 8134, St. Louis, MO, 63110*, Roger F. Haskett, W. Vaughn McCall, Joan Prudic, Katherine J. Pierce, Ph.D., Harold A. Sackheim

Educational Objectives:

After reviewing this presentation the participant should be able to recognize from this blinded study that the risks associated with the concurrent administration of venlafaxine or nortriptyline and electroconvulsive therapy are minimal.

Summary:

The risks of the concurrent administration of antidepressants during a course of ECT are largely unclear because of a paucity of information. This abstract reports initial findings from a multi-site trial in which 338 patients were randomly assigned to take either nortriptyline, venlafaxine or placebo during acute ECT in a blinded fashion (Sex: 64% women, 36% men; Race: 91% Caucasian, 7% African-American, 1% Native American, 1% Asian; Age: X = 49.3, SD = 15.8). Patients were also randomized to right unilateral (RUL) or bilateral (BL) ECT with raters and patients blinded to treatment status. Side effects were systematically ascertained using the Udvalg for Kliniske Undersøgelser (UKU) Side Effect Rating Scale. Serious Adverse Events (SAE's- N = 13) and Adverse Events (AE's - N = 21) were also documented. The SAE's and AE's were equally distributed among patients receiving nortriptyline, venlafaxine and placebo. Similarly, AE's and SAE's were equally distributed among RUL and BL stimulus patients. A preliminary analysis of common venlafaxine associated side effects (nausea, diarrhea and tremor) suggests that the frequency of these side effects were statistically indistinguishable among patients receiving venlafaxine, nortriptyline and placebo. Further analysis will be presented to support the preliminary impression that neither venlafaxine nor nortriptyline obviously complicated the administration of ECT.

References:

1. Gonzalez-Pinto A, Gutierrez M, Gonzalez N, Elizagarate E, Perez de Heredia JL, Mico JA. Efficacy and safety of venlafaxine-ECT combination in treatment-resistant depression. J Neuropsychiatry Clin Neurosci 2002; 14(2):206-209.
2. Kellner CH, Nixon DW, Bernstein HJ. ECT-drug interactions: A review. Psychopharmacol Bull 1991; 27(4):595-609.

NR519 Tuesday, May 23, 3:00 PM - 5:00 PM

Quality Outcomes in Treated Depression: A Study of a Rural Sample in Southern India

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Educational Objectives:

1. Participants will appreciate the epidemiology of Major Depression in rural Southern India
2. Participants will review outcomes as determined by analyses of data gathered using international instruments

Summary:

The National Mental Health Programme in India was developed to address the problem of mental illnesses, especially in rural areas. However, it has been criticized for emphasizing the identification and treatment of only severe mental disorders such as psychoses, while not addressing Common Mental Disorders [CMD], which are equally disabling.

CMD, which are neurotic disorders presenting with anxiety and depressive symptoms, are widespread and are known to cause significant disability worldwide. In India, prevalence rates of CMD range from 2% to 57% .

This paper describes the outcomes of treated anxiety and depression in 196 attendees at a community mental health programme which is integrated with primary health care services, rendered in a rural area and that addresses CMD alongside psychotic disorders and epilepsy.

Continuous variables were analyzed using independent samples t test, while for categorical variables chi square test was employed. Logistic regression analysis was used to examine the relationship between clinical and demographic variables and outcome. All tests were done using SPSS version 13. The significance level was set at p< .05.

Results show 35% of patients in complete remission at 6 months; a significant proportion of patients had poor outcome with score of >7 on the Hamilton Depression Rating Scale. Individuals with a higher score on WHO QOL Bref had a poorer quality of life. The presence of co-morbid psychiatric and medical conditions and ongoing life stressors were associated with poor outcome.

References:

1. Sen B, Williams P.(1987). The extent and nature of depressive phenomena in primary health care: A study in Calcutta, India. British Journal of Psychiatry, 151; 486-493.

2. Goldberg D, Lecruiber Y. (1995). Form and frequency of mental disorders across cultures. In: Ustun TB, Sartorius N (Eds). Mental Illness in general health care: an International study. John Wiley & Sons; 323-334.

NR520 Tuesday, May 23, 3:00 PM - 5:00 PM

Asenapine Improves Cognitive Function in Monkeys Repeatedly Exposed to the Psychotomimetic Drug Phencyclidine

J. David Jentsch, Ph.D. *University of California at Los Angeles, Department of Psychology, PO Box 951563, Los Angeles, CA, 90095-1563*, Mohammed Shahid, Ph.D., Erik H.F. Wong, Ph.D., Robert H. Roth, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to:

1. Describe the model of PCP-induced cognitive impairment in monkeys and its usefulness in determining the efficacy of psychopharmacologic agents for cognitive dysfunction.
2. Discuss the effects of asenapine on cognitive function in monkeys with PCP-induced cognitive impairment.

Summary:

Objective: Long-term exposure to the *N*-methyl-D-aspartate/glutamate-receptor antagonist phencyclidine (PCP) impairs cognitive and executive functions in animals, potentially modeling important endophenotypes for schizophrenia. Administering atypical antipsychotics to chronic PCP-exposed monkeys produces small gains in reversal learning and object retrieval, supporting the validity of this model in discerning therapeutic drug effects on cognitive function. Asenapine is a novel psychopharmacologic agent under development for treating schizophrenia and bipolar disorder. We explored the effects of short- and long-term asenapine dosing on reversal learning (measure of response switching) and object retrieval (measure of response inhibition) in normal and chronic PCP-exposed monkeys.

Methods: Forty-eight monkeys were trained to perform reversal learning and object retrieval procedures before BID dosage with PCP (0.3 mg/kg intramuscular) or saline for 14 days. A baseline test confirmed cognitive deficits in PCP-exposed animals before beginning BID subcutaneous administration of saline (control) or asenapine (50, 100, or 150 μg/kg).

Results: In the reversal task, PCP-exposed monkeys made more perseverative Extended Release rors than did control subjects, evidence of poor capacity to switch responses. On average, PCP-treated monkeys made twice as many Extended Release rors as did control monkeys under these conditions. Asenapine facilitated reversal learning performance in PCP-exposed monkeys. Improvements in reversal learning were at the trend level in week 1, became significant in week 2, and remained significant through week 4. Specifically, in week 4, asenapine 150 μg/kg significantly improved reversal learning in PCP monkeys (P=0.01), rendering their performance indistinguishable from that of normal monkeys.

Conclusions: Asenapine produced substantial gains in executive functions in this model of cognitive dysfunction that were maintained with long-term dosing. The cognition-enhancing properties of asenapine may be, at least in part, attributed to its unique human receptor signature, characterized by strong affinity for serotonergic, dopaminergic, and alpha-adrenergic receptors.

Funding Source: This study was supported by Organon Laboratories Ltd and Pfizer Inc.

References:

1. Jentsch JD, Redmond DE, Elsworth JD, Taylor JR, Youngren KD, Roth RH: Enduring cognitive deficits and cortical dopamine dysfunction after long-term administration of phencyclidine to monkeys. Science 1997; 277: 953-955.
2. Jentsch JD, Taylor JR, Redmond DE, Elsworth JD, Youngren KD, Roth RH: Dopamine D4 receptor antagonist reversal of subchronic phencyclidine-induced object retrieval/detour deficits in monkeys. Psychopharmacology 1999; 142:78-84.

NR521 Tuesday, May 23, 3:00 PM - 5:00 PM

Serotonin Transporter Occupancy in Rats Exposed to Fluoxetine in Utero or Via Breast Milk

Catherine F.C. Jones *Emory University, 101 Woodruff Circle, Rm 4007, Atlanta, GA, 30322*, Zachary N. Stowe, Michael J. Owens

Educational Objectives:

At the conclusion of this presentation, the participant should be better informed about *in utero* CNS fluoxetine exposure and postpartum clearance rates. The participant should realize that fluoxetine SERT occupancy is equal between the dam and fetus and takes at least fifteen days postpartum to clear entirely. Although the adult rats exposed prenatally showed no change in motor skills, innate anxiety, or SERT density measurements, more studies are needed to assess long-term effects of prenatal and neonatal SSRI exposure. This data will lead to better informed guidelines aimed at minimizing said exposure.

Summary:

Objective: Data regarding the CNS effects of *in utero* antidepressant exposure, neonatal CNS clearance, and exposure *via* breast milk is sparse. Using an animal model, the magnitude of fluoxetine exposure was measured in four groups: (1) *in utero*, (2) postnatal clearance of, (3) exposure through lactation, and (4) longitudinal studies.

Methods: Rats were exposed to fluoxetine (by osmotic minipump) *in utero* or postnatally *via* breast milk. Dam dosing reflected the 50th and 85th percentile of clinical serum concentrations in pregnant women. Serum drug concentrations were assayed by HPLC and pup 5HT transporter (SERT) occupancy was measured by *ex vivo* autoradiography. Adult rats, exposed to fluoxetine prenatally, were assessed in the beam traversing and open field tasks. Adult SERT density was measured in a radioligand binding assay.

Results: Embryonic day 21 (E21) rat pups exposed to fluoxetine *in utero* exhibited >95% SERT occupancy. By postnatal day 4, SERT occupancy had significantly decreased but was still measurable on postnatal day 8. NaUïve pups were exposed to fluoxetine *via* breast milk exhibited ~40-60% SERT occupancy in 4 and 8 day old rat brains. Longitudinal studies (beam traversing and open field task, SERT density measurement) showed no differences between groups.

Conclusions: These data show that the magnitude of fluoxetine exposure *in utero* was equivalent between dams and the fetuses and that complete clearance required at least 15 days. Significantly less, but measurable, exposure occurred via breast milk exposure. No differences in motor skills, anxiety or SERT density were observed in adulthood following *in utero* exposure. SSRIs have proven extremely valuable in the treatment of pregnant and nursing women; nevertheless further modeling of drug exposure in infants combined with CNS measures will enhance guidelines which can be used to systematically minimize fetal and neonatal medication exposure. Supported by NIH P50 MH 68036.

References:

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2. Vartazarmian R, Malik S, Baker GB, Boksa P. Long-term effects of fluoxetine or vehicle administration during pregnancy on behavioral outcomes in guinea pig offspring. Psychopharmacology (Berl). 2005 Mar;178(2-3):328-38.

NR522 Tuesday, May 23, 3:00 PM - 5:00 PM

Polymorphisms of Dysbindin Gene (DTNBP1) and Schizophrenia in the Korean Population

Tae-Youn Jun, M.D. *St. Mary's Hospital, Psychiatry, 62 Yoido-dong, Youngdeungpo-gu, Seoul, 150-713, Republic of Korea*, Won-Myong Bahk, M.D., Jeong-Ho Chae, M.D., Chi-Un Pae, M.D., Young-Eun Jung, M.D., Byung-Wook Lee, M.D., Seung-Kyu Bang, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to demonstrate that DTNBP1 can be a susceptibility gene for schizophrenia in the Korean population.

Summary:

Objectives: The gene encoding the dystrobrevin binding protein (DTNBP1) has been implicated in the pathogenesis of schizophrenia by several association studies. The dysbindin gene is located at chromosome 6p22.3, one of the most promising susceptibility loci in linkage studies of schizophrenia. The aim of this study is to determine whether DTNBP1 is associated with schizophrenia in the Korean population.

Method: 452 Korean patients with schizophrenia in accordance with DSM-IV criteria and 442 Korean healthy individuals matched to age and sex participated in this study. We examined two single nucleotide polymorphisms (p1635, p1325) using Pyrosequencing system, and examined allele, genotype and haplotype association with schizophrenia.

The results were analyzed by chi-square test and Fisher's exact test.

Results: There were no significant differences in genotype and allelic frequencies of SNP p1635 between cases and controls ($\chi 2 = 1.21$, df=2, p=0.655, $\chi 2 = 0.575$, df=1, p=0.448). However, SNP p1325 reached significance. The frequency of the rare allele was significantly higher in cases compared with controls ($\chi 2 = 6.35$, df=2, p=0.042, $\chi 2 = 4.41$, df=1, p=0.036). Two SNP haplotype AC, GC were not associated with schizophrenia, but SNP haplotype AT was significantly in excess in cases compared with controls. ($\chi 2 = 4.41$, df=1, p=0.036)

Conclusion: These results provide the support for DTNBP1 as a susceptibility gene for schizophrenia in the Korean population. In the future, further studies should be needed to confirm the relationship between genetic variation in DTNBP1 and the phenotype of schizophrenia.

Key Words: Schizophrenia, Dysbindin gene (DTNBP1), Polymorphism.

References:

1. Williams NM, Preece A, Morris DW, Spurlock G, Bray NJ, Stephens M, et al: Identification in 2 independent samples of a novel schizophrenia risk haplotype of the dystrobrevin binding protein gene (DTNBP1). Arch Gen Psychiatry. 2004;61:336-344.

2. Kirov G, Ivanov D, Williams NM, Preece A, Nikolov I, Milev R. Strong evidence for association between the dystrobrevin binding protein 1 gene (DTNBP1) and schizophrenia in 488 parent-offspring trios from Bulgaria. Biol Psychiatry. 2004;55:971-975.

NR523 Tuesday, May 23, 3:00 PM - 5:00 PM

Concomitant Use of Anticholinergic Agents With Atypical Antipsychotics in Schizophrenic Patients

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to judge the adequacy of the anticholinergic medication used in clinical trials.

Summary:

Objectives: Antipsychotic drugs induce extrapyramidal symptoms such as dystonia, akathisia and parkinsonian symptoms early in the treatment. With the advent of atypical antipsychotic drugs, the incidence of extrapyramidal symptoms has decreased, but danger still exists. Hence, in treatment of schizophrenia with antipsychotics, anticholinergic agents are often indicated.

Methods: In this observation, retrospective study, we examined whether the initiation of risperidone, olanzapine, or quetiapine, the three most widely prescribed atypical antipsychotics, is related to the concomitant use of anticholinergic agents. We identified patients with schizophrenia from outpatient clinics in the St. Mary's hospital and defined initiation of risperidone, olanzapine, or quetiapine as patients who initiated on the target drug after January 1 2004 and continuously use the antipsychotics for 6 months. The data were analysed using on way ANOVA, Mann-Whitney U test or Fisher's exact tests.

Results: The study yield two major findings. First, compared with risperidone initiators, there were significantly fewer olanzapine initiators who used anticholinergic agent concomitantly. Secondly, there were significantly fewer olanzapine or quetiapine initiators than risperidone initiators who prescribed anticholinergic agent on the same day when antipsychotics was initiated.

Conclusions: As the use of anticholinergic agent is a proxy for the presence of extrapyramidal symptom, these findings suggest that risperidone may be more associated with extrapyramidal symptoms than olanzapine or quetiapine. Controlled studies comparing them to one another should be of particular interest.

References:

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2. Burgyone K, Aduri K, Ananth J, Parameswaran S: The use of antiparkinsonian agents in the management of drug-induced extrapyramidal symptoms. Curr Pharm Des. 2004;10(18):2239-48.

NR524 Tuesday, May 23, 3:00 PM - 5:00 PM

A Survey to Examine Psychiatrist's Attitudes and Patterns of Antipsychotic Prescribing Practices for Schizophrenia in the U.S. and Japan

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the US and Japanese psychiatristsâ€™ understanding of pharmacological treatment for schizophrenia.

Summary:

BACKGROUND: The aim of this study was to clarify the reason for the difference in prescription rates of second generation antipsychotic drugs (SGA) between the USA and Japan. METHODS: We conducted a mail survey in the USA and Japan. As a result, 183/777 (23.6%) US and 240/619 (38.8%) Japanese psychiatrists responded. RESULTS: 1) Over 50% of both US and Japanese respondents chose risperidone as a main drug for the treatment of positive symptoms. For negative symptoms, risperidone (35%) was most popular in the USA, and olanzapine (38%) in Japan. For maintenance treatment, over 50% of both US and Japanese respondents chose risperidone. For treatment-resistant schizophrenia, over 50% of US respondents chose clozapine as a main drug. In contrast, nearly 40% of Japanese respondents chose olanzapine in Japan. For suicidal behavior, clozapine was most popular in the USA, and risperidone in Japan. For themselves and their family, risperidone was most popular in both the USA and Japan. 2) Around two-thirds of the US and Japanese respondents answered that they sometimes switched patients from first generation antipsychotic drugs (FGA) to SGA. 3) Around 50% of the US and Japanese respondents answered that they sometimes used combinations of antipsychotic drugs. 4) Comparing to Japanese respondents, US respondents chose more factors which would affect the choice of medications. 5) As a medical resource, Journal articles and own experiences were popular in both countries. 6) Around 80% of the US and Japanese respondents answered that the prescription rate of SGA in Japan is low. Meanwhile, over 50% of the US and Japanese respondents answered the prescription rate of SGA in the USA is fair. CONCLUSIONS: Except for schizophrenia with suicidal behavior, the choice of SGA was common even among Japanese psychiatrists.

References:

1. Steinert T: Which neuroleptic would psychiatrists take for themselves or their relatives? Eur Psychiatry 2003; 18:40-41.
2. Takei N, Inagaki A: Polypharmacy for psychiatric treatments in Japan. Lancet 2002; 360:647.

NR525 Tuesday, May 23, 3:00 PM - 5:00 PM

The Effect of Risperidone Oral Solution on Schizophrenic Patients Who Respond Poorly to Normal Formula of Risperidone

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to treat schizophrenic patients.

Summary:

Recently, risperidone oral solution (RIS-OS) was developed to treat the acute phase of schizophrenic patients. Patients taking RIS-OS sometimes report that they feel better than when they take tablets of risperidone (RIS) in daily clinical practice. In this study, we substituted RIS-OS for patients showing insufficient response to RIS and evaluated the therapeutic effects by serial BPRS (Brief Psychiatry Rating Scale), DIEPSS (Drug-induced Extrapyramidal Sign Scale), and CGI (Clinical Global Impression) at the time of the switch, and 2, 4, 8 and 12 weeks after the switch. Subjects were five schizophrenic patients in the F2 category on ICD-10, who showed insufficient response to RIS. After switching from RIS to an equivalent dose of RIS-OS, the dose of RIS-OS was adjusted to the patient's symptoms. Twelve weeks later, the BPRS total score was markedly decreased in two cases, slightly in two and was unchanged in one. In two patients showing remarkable improvement, scores of impulsivity/hostility on BPRS showed a significant decrease. EPS seen in three patients before switching disappeared following the substitution and two other patients, who did not have EPS, did not develop EPS after 12 weeks of RIS-OS. Regarding CGI global improvement, prominent improvement and slight improvement were seen in 2 cases each. One patient did not show any change. The results suggested that RIS-OS is one of the useful choices in the treatment of schizophrenic patients who respond poorly to RIS. The mechanism of differences in the effects of RIS-OS and RIS is discussed.

References:

1. Gutierrez R, Lee PI, Huang ML, Woestenborghs R: Risperidone: effects of formulations on oral bioavailability. Pharmacotherapy 1997; 17:599-605.
2. Currier GW, Simpson GM: Risperdone liquid concentrate and oral lorazepam vesus intramuscular haloperidol and intramuscular lorazepam for treatment of psychotic agitation. J Clin Psychiatry 2001; 63:153-157.

NR526 Tuesday, May 23, 3:00 PM - 5:00 PM

Risperidone Augmentation for Patients With Difficult-to-Treat Major Depression

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the availability of new pharmacological options in the management of patients with difficult-to-treat depressions.

Summary:

97 patients who met criteria for unipolar nonpsychotic major depression and failed to respond or partially responded to an adequate trial of antidepressant medication were randomized to receive adjunctive risperidone or placebo for an additional 4-week double-blind treatment trial. Outcome was determined by a Montgomery-Asberg Depression Rating Scale (MADRS) rating ≤ 10 to denote remission. Secondary outcomes included Hamilton Rating Scale for Depression (HRSD) scores, Clinical Global Impression (CGI) ratings, adverse events, and quality-of-life ratings (Q-LES-Q).

Baseline severity of depression was comparable between patients receiving risperidone or placebo augmentation. Modified ITT analysis showed that subjects in both groups improved significantly over time in the MADRS scores, but the odds of remitting were significantly better for patients in the risperidone treatment group (OR = 3.33, 95% CI = 1.303, 8.526, p=.011). At the end of four weeks of treatment 51.6% of the risperidone augmentation group remitted compared to 24.2% of the placebo augmentation group (CMH (1) = 6.48, p=.011). Results of HRSD scores showed that 35.5% of the risperidone augmentation group remitted (HRSD ≤ 7) compared to 18.2% of the placebo group (CMH (1) = 3.10, p=.078). CGI change scores also improved for both groups but did not reach between-group significance (F (1,91) = 2.92, p= .091). There was no significant difference between groups in the overall number of adverse events reported. Overall quality-of-life and satisfaction with medication improved over time between groups, with patients in the risperidone group reporting significantly better scores compared to the placebo group (F (1,62) = 6.44, p= .014).

Augmenting an antidepressant with risperidone for patients with difficult-to-treat depression leads to a significantly higher remission rate, significantly better quality-of-life, significantly better odds

of remission without an increase in overall side effect burden. Augmentation with risperidone appears to be an efficacious treatment option for patients with difficult-to-treat depression.

References:

1. Shelton RC, Tollefson GD, Tohen M, et al: A novel augmentation strategy for treating resistant major depression. American Journal of Psychiatry 158:131-134, 2001.
2. Fleck M, Howarth E: Pharmacologic management of Difficult-to-treat depression in clinical practice. Psychiatric Services 56:(8):1005-1011, 2005.

NR527 Tuesday, May 23, 3:00 PM - 5:00 PM

Assessing Recurrence Prevention: A Placebo-Controlled Trial of Venlafaxine XR in Patients With Recurrent Unipolar Major Depression

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to:

1. Assess the efficacy and safety of venlafaxine XR compared with placebo in the prevention of recurrence of major depressive disorder
2. Evaluate the efficacy and safety of venlafaxine XR versus placebo in maintenance treatment of major depressive disorder
3. Discuss methods used in measuring the rate of recurrence of major depressive disorder

Summary:

Background: Two-year maintenance phase study to evaluate long-term efficacy and safety of venlafaxine (Effexor®) extended release (XR) in preventing recurrence of depression.

Methods: Patients (N=1096) were randomly assigned in a 3:1 ratio to 10-week treatment with venlafaxine XR (75-300 mg/day) or fluoxetine (20-60 mg/day). Responders (HAM-D_{17} total score ≤12 and ≥50% decrease from baseline) entered a 6-month, double-blind continuation phase on the same medication. Continuation phase responders enrolled into the maintenance phase consisting of 2 consecutive 12-month periods. At the start of each maintenance period, Venlafaxine XR responders were randomly assigned to receive double-blind treatment with Venlafaxine XR or placebo, and fluoxetine responders were continued for each period. We report results from the first 12-month maintenance period and compare the time to recurrence of depression with venlafaxine XR versus placebo. The primary definition of recurrence: HAM-D_{17} total score >12 and <50% reduction from baseline (acute phase) HAM-D_{17}.

Results: The cumulative probabilities of recurrence through 12 months in the venlafaxine XR (n=164) and placebo (n=172) patients who had been responders to Venlafaxine XR during the continuation phase were 23.1% (95% CI: 15.3, 30.9) and 42.0% (95% CI: 31.8, 52.2), respectively (cumulative recurrence comparison P=0.005, log rank test).

Conclusion: Twelve-month venlafaxine XR maintenance treatment was effective in preventing recurrence of depression in patients successfully treated with venlafaxine XR during acute and continuation therapy.

References:

1. Montgomery SA, Entsuah R, Hackett D, Kunz NR, Rudolph RL: Venlafaxine versus placebo in the preventive treatment of recurrent major depression. J Clin Psychiatry 2004; 65:328-336.
2. Gilaberte I, Montejo AL, de la Gandara J, Perez-Sola V, Bernardo M, Massana J, Martin-Santos R, Santiso A, Noguera R, Casais L, Perez-Camo V, Arias M, Judge R; Fluoxetine Long-Term Study Group: Fluoxetine in the prevention of depressive recurrences:.

NR528 Tuesday, May 23, 3:00 PM - 5:00 PM

Recurrence Prevention: Efficacy of Two Years of Maintenance Treatment With Venlafaxine XR in Patients With Recurrent Unipolar Major Depression

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to:

1. Compare the efficacy of venlafaxine XR and placebo in the prevention of recurrence of MDD
2. Evaluate the safety and tolerability of venlafaxine XR versus placebo in maintenance treatment of MDD
3. Discuss methods used in assessing recurrence of MDD

Summary:

Background: Second-year maintenance phase from a 4-phase long-term study to evaluate efficacy and safety of venlafaxine (Effexor®) extended release (XR) in preventing recurrence of depression.

Methods: Patients (N=1096) were randomly assigned in a 3:1 ratio to 10-week treatment with venlafaxine XR (75-300 mg/day) or fluoxetine (20-60 mg/day). Responders (HAM-D_{17} total score ≤12 and ≥50% decrease from baseline) entered a 6-month, double-blind continuation phase on the same medication. Continuation phase responders enrolled into the maintenance phase consisting of 2 consecutive 12-month periods. At the start of each maintenance period, venlafaxine XR responders were randomly assigned to receive double-blind treatment with venlafaxine XR or placebo, and fluoxetine responders were continued for each period. We report results from the second 12-month maintenance phase, which compared the time to recurrence of depression with venlafaxine XR versus placebo, as its primary efficacy measure. The primary definition of recurrence was a HAM-D_{17} total score >12 and <50% reduction from baseline (acute phase) HAM-D_{17} at 2 consecutive visits or at the last valid visit prior to discontinuation.

Results: The cumulative probabilities of recurrence through 12 months in the venlafaxine XR (n= 43) and placebo (n= 40) patients who had been responders to venlafaxine XR during the first maintenance phase were 8.0 % (95% CI: 0.0, 16.8) and 44.8% (95% CI: 27.6, 62.0), respectively (P<0.001, log rank test). Overall discontinuation rates were 28% and 63% in the venlafaxine XR and placebo groups, respectively. Adverse events were the primary reason for discontinuation for 1 patient (2%) in the venlafaxine XR group and 4 (10%) in the placebo group.

Conclusion: An additional 12 months of maintenance therapy with venlafaxine XR was effective in preventing recurrence of depression in patients who had been responders to venlafaxine XR during acute, continuation, and 12 months of maintenance therapy.

References:

1. Montgomery SA, Entsuah R, Hackett D, Kunz NR, Rudolph RL: Venlafaxine versus placebo in the preventive treatment of recurrent major depression. J Clin Psychiatry 2004; 65:328-336.

2. Gilaberte I, Montejo AL, de la Gandara J, Perez-Sola V, Bernardo M, Massana J, Martin-Santos R, Santiso A, Noguera R, Casais L, Perez-Camo V, Arias M, Judge R; Fluoxetine Long-Term Study Group: Fluoxetine in the prevention of depressive recurrences:.

NR529 Tuesday, May 23, 3:00 PM - 5:00 PM

Citalopram for Depressive Symptoms in Chronic Schizophrenia

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that citalopram is useful and safe as a treatment for depressive symptoms in schizophrenia.

Summary:

Objectives

There is increasing evidence suggesting that depressive symptoms may be associated with serotonergic dysfunction in schizophrenic patients. This study aimed to determine the efficacy and safety of citalopram as a treatment for depressive symptoms in patients with chronic schizophrenia.

Method

The Calgary Depression Scale for Schizophrenia(CDSS) was used as the outcome measure. Forty-seven patients suffering from schizophrenia(DSM-IV) with CDSS scores higher than 8 were included in a double-blind, placebo-controlled, 8-week trial of citalopram. Citalopram was started at 20 mg/day; this could be increased to 40 mg after 4 weeks for an inadequate response.

Results

There were no significant differences between these two groups with respect to age education, gender, type of antipsychotic and baseline CDSS scores. There was no significant difference in the mean score on the CDSS at baseline(citalopram group versus placebo group = 9.840 +/- 2.192 versus 9.272 +/- 1.579, p=0.320). But after 8 weeks there was a significant difference in the mean CDSS score between two groups(citalopram group versus placebo group = 6.080 +/- 1.824 versus 7.818 +/- 1.816, p=0.002). No clinically significant adverse effects were reported by the patients or observed by the examiner.

Conclusion

The results suggest that citalopram is useful and safe as a treatment for depressive symptoms in schizophrenia.

References:

1. Shim JC, Kelly DL, Kim YH, Yoon YR, Park JH, Shin JG, Conley RR:Fluoxetine augmentation of haloperidol in chronic schizophrenia.J Clin Psychopharmacol. 2003 Oct;23(5):520-2.
2. Anghelescu I, Szegedi A, Schlegel S, Weigmann H, Hiemke C : Combination treatment with clozapine and paroxetine in schizophrenia: safetyand tolerability data from a prospective open clinical trial.Eur Neuropsychopharmacol. 1998 Dec;8(4):315-20.

NR530 Tuesday, May 23, 3:00 PM - 5:00 PM

Direct Transition to Long-Acting Risperidone: Long-Term Efficacy

Werner Kissling, M.D. *Klinikum rechts der Isar, Klinik und Poliklinik für Psychiatrie und Psychotherapie, Möhlstrae 26, Muenchen, Germany, 81675, Germany*, Stephan Heres, M.D., Keith Lloyd, M.D., Emilio Sacchetti, M.D., Philippe Bouhours, M.D., Rossella Medori, M.D., Pierre-Michel Llorca, M.D.

Educational Objectives:

This poster informs the reader that the long-acting injectable atypical antipsychotic provides good long-term (12 month) efficacy for treatment of patients with schizophrenia and other psychotic disorders.

Summary:

Objective: To investigate the efficacy and safety of long-acting risperidone (RLAI) during a 12 month period in patients with schizophrenia and other psychotic disorders.

Methods: Symptomatically stable patients requiring medication change were enrolled. Psychopathology was assessed using PANSS at baseline, and after 1, 3, 6, 9 and 12 months treatment with RLAI. Remission was assessed according to Remission in Schizophrenia Working Group guidelines.

Results: Of 715 patients (63% male), 508 (71%) completed the 12 month study. Mean PANSS total score was significantly reduced from baseline (74.9 ± 22.7) to endpoint (59.7 ± 21.9, $p<0.001$). 31% of the patients who did not meet the PANSS severity criteria for remission at baseline improved and fulfilled the criteria for sustained remission (being in remission for at least 6 months) during the trial. The proportion of patients meeting PANSS severity criteria for remission rose from 29% at baseline to 60% (429 patients) at endpoint. Only few patients discontinued due to tolerability problems. Most commonly reported treatment-emergent adverse events were anxiety (12%), insomnia (10%), and weight-gain (8%).

Conclusion: Treatment with RLAI for 12 months resulted in significant and sustained improvements in symptom control. Improvements enabled patients to achieve and maintain 6 month remission from their symptoms.

References:

1. Andreasen NC, Carpenter WT, Jr., Kane JM, Lasser RA, Marder SR, Weinberger DR. Remission in schizophrenia: proposed criteria and rationale for consensus. Am J Psychiatry 2005;162(3):441-9.
2. Moeller H, Llorca P, Sacchetti E, Martin S, Medori R, Parellada E. Efficacy and safety of direct transition to risperidone long-acting injectable in patients treated with various antipsychotic therapies. Int Clin Psychopharmacol 2005;20(3):121-130.

NR531 Tuesday, May 23, 3:00 PM - 5:00 PM

Measurements of Anterior Cingulate Cortex Volumes in Combat-Related PTSD: Twin Study

Noriyuki Kitayama, M.D. *National Center of Neurology and Psychiatry, Japan, Division of Adult Mental Health, 4-1-1 Ogawahigashi-cho, Kodaira-shi, Tokyo, 187-8553, Japan*, Nadeem Afzal, M.D., Faiz A. Cheema, M.D., Ali Ashraf, M.D., Sinead C. Quinn, B.S., Lai Reed, M.B.A., Marijn Brummer, Ph.D, Viola Vaccarino, M.D., Yoshiharu Kim, M.D., Jack Goldberg, Ph.D., James D. Bremner, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize *brain morphological changes in posttraumatic stress disorder* and also the effects on brain tissue by chronic stress. In addition, my current study will suggest the reductions of the anterior cingulate cortex volume in PTSD may be required pathological change.

Summary:

Introduction: In a recent animal study, repeated restraint stress induced apical dendritic reorganization in the anterior cingulate cortex (ACC). Studies in patients with posttraumatic stress disorder (PTSD) also showed smaller volume of the ACC. However, those human studies do not address whether the changes are

stress-related or are related to a pre-existing difference in brain structure. These questions can be addressed in longitudinal and/or twin studies. The purpose of the current study was to clarify whether the structural changes of ACC were required or acquired in subjects with combat-related PTSD in Vietnam-era.

Methods: MRI was used to measure the ACC volume in 9 male pairs of twins which involved each of them with and without combat-related PTSD. **Results:** The absolute volume of ACC in twins with PTSD: Rt. 6650.0 +/- 897.4; Lt. 6778.9 +/- 1112.0. Their brothers without PTSD: Rt. 7460.4 +/- 1529.6; Lt. 7260.3 +/- 1348.2 (mm^3; AVE +/- STD). ACC volume on the right side in PTSD was significantly reduced by 7.8% in comparison to non-PTSD (p=0.02). **Conclusions:** This preliminary data suggests reductions of ACC volume in PTSD was required pathological change. Data in the complete sample of greater than 20 subjects will be presented.

References:

1. Kitayama N, Quinn S, Bremner JD: Smaller Volume of Anterior Cingulate Cortex in Abuse-Related Posttraumatic Stress Disorder. J Affect Disord 2005 (in press).
2. Woodward SH, Kaloupek DG, Streeter CC, Martinez C, Schaer M, Eliez S: Decreased Anterior Cingulate Volume in Combat-Related PTSD. Biol Psychiatry 2005 (in press).

NR532 WITHDRAWN

NR533 Tuesday, May 23, 3:00 PM - 5:00 PM

Coping Strategies Within Major Depressive Disorder

Brian Y. Kong *START Clinic, 1 Lonsdale Court, Unionville, ON, L3R7T6, Canada*, Madalyn Marcus, Leslie Jacobs, Grace Son, Monica Vermani, Martin Katzman

Educational Objectives:

At the conclusion of this presentation, the participant should be able to demonstrate that depressed patients employ poor coping strategies for dealing with stressful situations. Furthermore, additional examination of subjects following Cognitive Behavioural Therapy (CBT) may provide a mechanism of predicting outcome in the treatment of MDD. In effect this should lead to more effective assessment and treatment of depressed patients.

Summary:

Coping Strategies Within MDD

MDD (MDD) reportedly affects 17.1% of the population, and costs approximately $44 billion annually.

Various psychological factors such as early traumatic experiences and terminal illness have been demonstrated as predictors of MDD. Other subsequent disorders such as substance abuse and eating disorders have also been associated with depression.

This study involved assessing the relationship between depression and coping strategies in patients referred to a tertiary care clinic. Patients referred to the clinic received a questionnaire package consisting of several scales assessing different patient variables. This included the Beck Depression Inventory II (BDI-II), and the Coping Inventory for Stressful Situations (CISS). The CISS assesses both less-adaptive coping strategies (i.e., emotional-oriented coping), and adaptive coping strategies (i.e., task-oriented coping). Less-adaptive coping strategies have been associated with less-adaptive personality traits and psychological distress, while adaptive coping strategies have been associated with adaptive personality traits and lack of distress.

We hypothesized that the scores of the BDI-II and CISS emotional-oriented subscale would be positively correlated, and that the scores of the BDI-II and CISS task-oriented subscale would be negatively correlated. Although preliminary (N=14, N=15), our data have produced a significant correlation of .595 (p-value .025) between the scores of the BDI-II and CISS emotional-oriented subscale, as well as a significant correlation of -.666 (p-value .007) between the scores of the BDI-II and the CISS task-oriented subscale. This provides further indication that depressed patients employ poor coping strategies for dealing with stressful situations. Furthermore, additional examination of subjects following Cognitive Behavioural Therapy (CBT) may provide a mechanism of predicting outcome in the treatment of MDD.

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1. Leivtan RD, et al. Major Depression in Individuals with a history of childhood physical or SExual abuse: relationship to neurovegetative features, mania, and gender. Am J Psychiatry 1998; 155:1746-1752.
2. McWilliams LA, Cox BJ, Enns MW. Use of Coping inventory for Stressful situations in a clinically depressed sample: factor structure, personality correlates, and prediction of distress. J Clin Psychol 2003; 59: 423-37.

NR534 Tuesday, May 23, 3:00 PM - 5:00 PM

Correlation Between Intolerance of Uncertainty and Perfectionism

Brian Kong *START Clinic, 1 Lonsdale Court, Unionville, ON, L3R7T6, Canada*, Madalyn Marcus, Martin Katzman

Educational Objectives:

At the conclusion of this presentation, the participant should be able to essentially demonstrate that both perfectionism and intolerance of uncertainty to serve as indicators of clinical anxiety disorders. This could ultimately lead to an improvement in both the assessment and treatment of anxiety disorders.

Summary:

Anxiety disorders have been reported to affect almost 25% of the population, with an estimated cost to the U.S. economy of over $40 billion per year. Hence psychological predictors of anxiety disorder severity have become a source of interest. Psychological factors predictive of the severity of mood and anxiety disorders such as adverse childhood events, and terminal illness have been previously investigated.

This study involved an assessment of uncertainty in its relationship to perfectionism in patients referred to a tertiary care clinic. Patients referred to the clinic received a questionnaire package assessing several different patient variables (including intolerance of uncertainty and perfectionism). Intolerance of uncertainty has been demonstrated to be an important construct in the process of worry, and has consequently been suggested as a contributing factor to anxiety disorders such as GAD. Perfectionism has been linked to irrational thinking (Flett et al., 1991), psychological stress, as well as anxiety disorders such as social phobia..

It was hypothesized that, as both having associations with anxiety disorder, the scores of the Intolerance of Uncertainty Scale (IUS) and Multidimensional Perfectionism Scale (MPS) would be positively correlated. Although the study is still in early stages of development (N=14), our findings have indicated a significant correlation of .556 (p-value .039) between the scores of the IUS and MPS. We believe that further research will strengthen this correlation, essentially demonstrating that both perfectionism and intolerance of uncertainty to serve as indicators of clinical anxiety disorders. This could ultimately lead to an improvement in both the assessment and treatment of anxiety disorders.

References:

1. Dugas MJ, Gosselin P, Ladouceaur R. Intolerance of Uncertainty and Worry: Investigating Specificity in a Nonclinical Sample. Cognitive Therapy and Research 2001; 25: 551-558.

2. McWilliams LA, Cox BJ, Enns MW. Use of Coping inventory for Stressful situations in a clinically depressed sample: factor structure, personality correlates, and prediction of distress. J Clin Psychol 2003; 59: 423-37.

NR535 Tuesday, May 23, 3:00 PM - 5:00 PM

A Fixed Dose Study of the Efficacy and Safety of Duloxetine for the Treatment of Generalized Anxiety Disorder

Hannu J. Koponen, M.D. *University of Oulu, P.O.Box 5000, Oulu, FIN-90014, Finland*, Christer Allgulander, M.D., Yili Pritchett, Ph.D., Janelle Erickson, Ph.D., Michael J. Detke, M.D., Susan G. Ball, Ph.D., James M. Russell, M.D.

Educational Objectives:

At the end of this presentation, participants will have knowledge about the efficacy and safety of duloxetine at 60 mg / day and 120 mg/ day for the treatment of generalized anxiety disorder.

Summary:

Objective: Both serotonergic and noradrenergic medications have been used independently for the treatment of GAD.[1] This study examined the efficacy and safety of duloxetine, a balanced and potent dual reuptake-inhibitor of 5HT and norepinephrine,[2] for treatment of GAD. *Methods*: In a 9-week, double-blind, fixed-dose study, 507 patients [Mean age=43.78 yrs; 67.8% female] with a DSM-IV defined GAD diagnosis were randomly assigned to receive duloxetine 60 mg/day (DLX-60mg, N=168), duloxetine 120 mg/day (DLX-120mg, N=170), or placebo (PBO, N=175). Primary efficacy outcome was change from baseline to endpoint in Hamilton Anxiety Scale (HAMA) total score assessed via ANCOVA. Secondary measures included response rate (≥50% HAMA reduction), mean change in Sheehan Disability Scale Global Functional Impairment score (SDS), and HAMA Psychic and Somatic Subscales. *Results:* Compared with PBO, both DLX groups demonstrated significantly greater reduction in HAMA scores (Mean decrease DLX-60mg=12.8, DLX-120mg=12.5, versus PBO=8.4, $P<.001$), greater response rates (DLX-60mg=58%, DLX120mg=56%, versus PBO=31%, $P<.001$), greater improvements in SDS global scores (Mean decrease DLX-60mg=7.8, DLX-120mg=7.0, versus PBO=3.8, $P<.001$), and greater reductions in the HAMA Psychic (Mean decrease DLX-60mg=7.6, DLX-120mg=7.1, versus PBO=4.5, $P<.001$) and HAMA Somatic subscales (Mean decrease DLX-60mg=5.2, DLX-120mg=5.3, versus PBO=3.8, $P<.001$) Discontinuation rates due to adverse events were 11.3% for DLX-60mg, 15.3% for DLX-120mg, versus 2.3% for PBO ($P<.001$). The three most frequent adverse events associated with duloxetine were nausea, dizziness, and dry mouth. *Conclusions*: Duloxetine 60mg and 120mg once daily was a safe, effective treatment that resulted in clinically significant improvement in symptom severity and disability associated with GAD.

References:

1. Baldwin DS, Polkinghorn C: Evidence-based pharmacotherapy of generalized anxiety disorder. Int J Neuropsychopharmacology 2005: 8:293-302.
2. Bymaster FP, Dreshfield-Ahmad LJ, Threlkeld PG, Shaw JL, Thompson L, Nelson DL,. Hemrick-Luecke SK, Wong DT: Comparative affinity of duloxetine and venlafaxine for serotonin and norepinephrine transporters in vitro and in vivo, human serotonin recept.

NR536 Tuesday, May 23, 3:00 PM - 5:00 PM

Eosinophilia Associated With Decreasing Neutrophil Count in Clozapine-Treated Psychiatric Patients

Tsuo-Hung Lan, M.D. *Yu-Li Hospital, DOH, Adult Psychiatry, 448 Chung-Hwa Road, Yu-Li, Hualien, 981, Taiwan Republic of China*, Hui-Ching Huang, B.Ph., Hsien-Jane Chiu, M.D., Che-Ling Yueh, M.D., El-Wui Loh, Ph.D., Tzong-Yuan Juang, M.D., Chin-Hsing Shu, M.P.H.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize a possible side effect from clozapine administration among schizophrenic patients. The eosinophilia might happen in two forms: subacute form and delayed form.

Summary:

Objective: Clozapine was known by its possible correlation with aplastic anemia in the literature review. However, another clinical observation, eosinophilia was found to be associated with a marked decline in neutrophil count in several case reports since 1980. We report five patients, during clozapine treatment, who developed severe eosinophilia. **Method:** Retrospectively, we reviewed 150 patients who were on clozapine therapy in some psychiatric hospital of Taiwan from May 1998 to July 2002. All subjects received regular whole blood cells series count and differential count of white cells weekly for 12 weeks, then followed once per 4 weeks afterwards. The stool smear was also examined for each subject to rule out the possible parasite infections. Any significant eosinophilia and neutropenia happened simultaneously will be record as an event. **Results:** Among the 150 cases, five patients developed eosinophilia associated with decreasing neutrophil count. On the basis of the literature, eosinophilia usually occurs between weeks3 and 5 of clozapine administration and disappears after another 4 weeks. Three of five patients showed this kind of subacute form of eosinophilia. However, two of the five patients developed eosinophilia in different time point after 1 year, and subsided 4 weeks later as well. **Conclusions:** This study indicates that schizophrenic patients who took clozapine might develop eosinophilia in 4 weeks after initiation of clozapine or 1 year after usage. The clinical indication of this kind of laboratory findings requires more exploration to clarify.

References:

1. Galletly C, Wilson D, McEwen S. Eosinophilia associated with decreasing neutrophil count in a clozapine-treated patient. J Clin Psychiatry. 1996;57(1):40-41.
2. Lucht MJ, Rietschel M. Clozapine-induced eosinophilia: subsequent neutropenia and corresponding allergic mechanisms. J Clin Psychiatry. 1998;59(4):195-197.

NR537 Tuesday, May 23, 3:00 PM - 5:00 PM

Efficacy and Tolerability of Indiplon in Primary Insomnia: Results of a Double-Blind, Placebo-Controlled, Four-Week Trial

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Educational Objectives:

The research data presented will contribute to the participant's understanding of the safety and efficacy of the treatment of DSM-IV primary insomnia.

Summary:

Introduction: The present study evaluated the efficacy and safety of indiplon, a novel Gamma-aminobutyric acid $_A$ receptor modulator, in adults diagnosed with primary insomnia characterized by sleep maintenance difficulties.

Methods: Patients (N=248) who met DSM-IV criteria for primary insomnia were randomized to 4 weeks of double-blind, nightly treatment with either indiplon 15mg or placebo. Subjective assessments included total sleep time (sTST, primary), wake time after

sleep onset (sWASO), number of awakenings after sleep onset (sNAASO), latency to sleep onset (LSO), and sleep quality. Responder status was defined as much-to-very-much improved on the Investigator Global Rating, Change scale (IGR-C).

Results: Treatment with indiplon was associated with significantly greater improvement than placebo on sTST over the 4 week treatment period (364.7 + 5.3 mins versus 336.6 + 5.3 mins; p=0.0002), as well as on all secondary sleep measures. Improvement in sleep onset and sleep maintenance parameters on indiplon was associated with significant improvement in sleep quality (p<0.0001) and a significantly higher rate of IGR-C responders (65% versus 33%; p<0.001). Indiplon was well-tolerated, with only somnolence occurring with an incidence of at least 5%, and greater than placebo (10.6% versus 4.1%).

Conclusions: The 15 mg dose of indiplon was safe and effective in inducing and maintaining sleep in patients with primary insomnia.

References:

1. Foster AC, Pelleymounter MA, Cullen MJ, Lewis D, Joppa M, Chen TK, Bozigian HP, Gross RS, Gogas KR. In vivo pharmacological characterization of indiplon, a novel pyrazolopyrimidine sedative-hypnotic. J Pharmacol Exp Ther 2004;311:547-559.
2. Simon GE, VonKorff M. Prevalence, burden, and treatment of insomnia in primary care. Am J Psychiatry 1997;154:1417-1423.

NR538 Tuesday, May 23, 3:00 PM - 5:00 PM

A Study on the Changes of Sexual Dysfunction After Substitution of a Setotonin Reuptake Inhibitor(SRI) With Bupropion Sustained Release in Major Depressive Disorder Patients With SRI-Induced Sexual Dysfunction

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Educational Objectives:

At the coclusion of this presentation, the participant should be able to recognize that substitution of serotonin reuptake inhibitor with bupropion-SR is one of the effective treatment strategies for patients with major depressive disorder and SRI-induced sexual dysfunction.

Summary:

Objectives : 5HT reuptake inhibitors(SRI), including SSRIs(SSRI) and venlafaxine, induce both therapeutic response and sexual dysfunction. This study was conducted to examine the changes in sexual dysfunction and depressive symptoms in the patients who had MDD and Sustained Release I-induced sexual dysfunction, after substitution of Sustained Release I with bupropion sustained release(SR).

Methods : This study included 14 married adults(9 men and 5 women) who had a DSM-IV-TR diagnosis of MDD in remission(Hamilton Rating Scale for Depression[HAM-D] score<11) and were receiving an Sustained Release I. Depression(using HAM-D) and sexual dysfunction(using Psychotropic-Related Sexual Dysfunction Questionaire[PRSexDQ]) were assessed at baseline, and bupropion Sustained Release was added to the current antidepressant. Sustained Release I was tapered off after 2 weeks from baseline and then bupropion Sustained Release monotherapy was tried after 4 weeks. HAM-D and PRSexDQ were assessed at 2 weeks, 4 weeks, 8 weeks from baseline. Paired sample T tests were performed to assess changes in depressive symptoms and sexual dysfunction

Results : Three patients withdrew from this study and 11patients(78.57%) completed the study. The patients showed no significant change from baseline to week 2, but sexual dysfunction decreased significantly from week 2 to week 4 and from week 4 to week 8. All patients showed no significant change in mean HAM-D scores during study period.

Conclusions : Substitution of Sustained Release I with bupropion Sustained Release is one of the effective treatment strategies for patients with MDD and Sustained Release I-induced sexual dysfunction.

References:

1. Woodrum ST, Brown CS: Management of SSRI-induced sexual dysfunction. Ann Pharmacother 1998;32:1209-1215.
2. Clayton AH, MeGarvey EL, Abouesh AI, Pinkerton RC: Substitution of an SSRI with bupropion sustained release following SSRI-induced sexual dysfunction. J Clin Psychiatry 2001;62:185-90.

NR539 Tuesday, May 23, 3:00 PM - 5:00 PM

Association Study of the Brain-Derived Neurotropic Factor Gene With Susceptibility to ADHD

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Educational Objectives:

The participant will understand the latest information in brain-derived neurotropic factor and attention deficit/hyperactivity disorder, and they also learn about the latest molecular genetic techniques.

Summary:

Objective: ADHD is a prevalent neurodevelopmental childhood psychiatric disorder. Several lines of evidence suggest that the gene coding for brain-derived neurotropic factor, *BDNF*, plays a role in the pathogenesis of ADHD: 1) drugs that control ADHD symptoms led to an elevation of brain BDNF mRNA levels in animal studies, 2) mice in which the *BDNF* gene was inactivated post-natally were hyperactive following exposure to stressors [(1)], 3) a family-based study demonstrated an association of the valine allele at the Val66Met polymorphism (rs6265) with ADHD [(2)]. The aim of the current study was to investigate *BDNF* for association with ADHD in an independent sample.

Method: The transmission of three polymorphisms of the *BDNF* gene (rs6265, rs11030104 and rs2049046) was examined in 266 nuclear families ascertained through a proband with ADHD (315 affected children) using the Transmission/Disequilibrium Test. In addition, we conducted quantitative analysis to assess the relationship between these marker alleles and the symptom dimensions of ADHD (inattention and hyperactivity/impulsivity) and cognitive measures of working memory.

Results: None of the individual marker alleles showed significant evidence of association with ADHD diagnosis, dimensional symptom scores, or working memory ability in our sample of ADHD families. There was no significant evidence for over-transmission of individual haplotypes with frequency >10% or the global χ^2 for these three haplotypes (χ^2=6.3491, df=3, P=0.096). But, one rare haplotype A-G-G (frequency 2.2%) showed a significant association with ADHD in categorical analysis (P=0.021) and quantitative analysis (parents' rated inattention: Z=2.504, P=0.012; hyperactivity/impulsivity: Z =2.651, P=0.008). However, these results have to be interpreted cautiously because of the low haplotype frequency. *Conclusions*: In the light of evidence for involvement of *BDNF* in ADHD, further analysis of the *BDNF* gene in ADHD is warranted.

References:

1. Rios M, Fan G, Fekete C, Kelly J, Bates B, Kuehn R, Lechan RM, Jaenisch R: Conditional deletion of brain-derived neurotrophic factor in the postnatal brain leads to obesity and hyperactivity. Mol Endocrinol 2001; 15:1748-1757.
2. Kent L, Green E, Hawi Z, et al: Association of the paternally transmitted copy of common Valine allele of the Val66Met polymorphism of the brain-derived neurotrophic factor (BDNF) gene with susceptibility to ADHD. Mol Psychiatry 2005; 10:939-943.

NR540 Tuesday, May 23, 3:00 PM - 5:00 PM

Quetiapine Regulates the Immobilization Stress-Induced BDNF and CRF Expression in Rat Brain

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Educational Objectives:

Quetiapine is a new atypical antipsychotic drug widely used in the treatment of schizophrenia.We used *in situ* hybridization to examine in rats the effects of chronic administration of quetiapine on chronic immobilization stress-induced changes in gene transcription. This study also examined the influence of quetiapine in an animal model of depression, the forced swimming test (FST). Repeated immobilization stress decreased mRNA levels of brain-derived neurotrophic factor (BDNF) in rat hippocampus ($p<0.01$). It increased mRNA levels of corticotropin-releasing factor (CRF) in the hypothalamic paraventricular nucleus (PVN) ($p<0.01$). Chronic quetiapine (10 mg/kg) treatment alone significantly increased BDNF mRNA expression by 10-32% ($p<0.05$) in the hippocampus when compared to controls. Furthermore, the stress-induced elevation of CRF mRNA expression was blocked by chronic quetiapine administration ($p<0.01$) although quetiapine treatment alone did not significantly reduce CRF mRNA levels in comparison to controls. At the conclusion of this presentation, the participant should be able to suggest that quetiapine has not only potentially an antidepressant effect but also a neuroprotective effect in schizophrenia and this effect may be related to its antipsychotic effect in patients with schizophrenia.

Summary:

Schizophrenia has been treated effectively with atypical neuroleptics without serious side effects. Long-term treatment with atypical neuroleptics is known to be correlated with an improvement of cognition in the patients with schizophrenia. Quetiapine is a new atypical antipsychotic drug widely used in the treatment of schizophrenia and other psychotic disorders. We used *in situ* hybridization to examine in rats the effects of chronic administration of quetiapine on chronic immobilization stress-induced changes in gene transcription. This study also examined the influence of quetiapine in an animal model of depression, the forced swimming test (FST). Repeated immobilization stress (2hr daily for 3 weeks) decreased mRNA levels of brain-derived neurotrophic factor (BDNF) in rat hippocampus ($p<0.01$). It increased mRNA levels of corticotropin-releasing factor (CRF) in the hypothalamic paraventricular nucleus (PVN) ($p<0.01$). Chronic quetiapine (10 mg/kg) treatment (daily for 3 weeks) alone significantly increased BDNF mRNA expression by 10-32% ($p<0.05$) in the hippocampus when compared to controls. Chronic administration of quetiapine also markedly increased the stress-induced decrease in BDNF mRNA ($p<0.01$). Furthermore, the stress-induced elevation of Corticotropin Releasing Factor mRNA expression was blocked by chronic quetiapine administration ($p<0.01$) although quetiapine treatment alone did not significantly reduce Corticotropin Releasing Factor mRNA levels in comparison to controls. When rats received acutely quetiapine (10, 20 and 40 mg/kg), quetiapine did reduce the immobility time at 10mg/kg, as compared with the control group ($p<0.05$) but it failed to reduce it at the highest dose tested (40 mg/kg). These results suggest that quetiapine has not only potentially an antidepressant effect but also a neuroprotective effect in schizophrenia and this effect may be related to its antipsychotic effect in patients with schizophrenia.

References:

1. . Bai O, Chlan-Fourney J, Bowen R, Keegan D, Li XM. Expression of Brain-Derived Neurotrophic Factor mRNA in Rat Hippocampus After Treatment With Antipsychotic Drugs. J Neurosci Res 2003;71:127-131.
2. Xu H, Qing H, Lu W, Keegan D, Richardson JS, Chlan-Fourney J, Li XM. Quetiapine attenuates the immobilization stress-induced decrease of brain-derived neurotrophic factor expression in rat hippocampus. Neurosci Lett. 2002;321:65-68.

NR541 Tuesday, May 23, 3:00 PM - 5:00 PM

A Comparison of Fractal Analysis of Resting EEG in Depressed Outpatients and Healthy Controls

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Educational Objectives:

The development of fractal analysis has provided useful tools in the study of physiological systems' activity. We compared the fractal analysis of resting EEG signal in depressed patients to a control group of healthy adult. This paper aim to search for a correlation between alterations in chaotic brain states and depressive disorders. Our results tentatively conclude that depressed patients have alterations in chaotic brain states. While the scaling exponents, which is the result of fractal analysis, in patients were closer to 1/f noise (scaling exponent = 1), controls were closer to white noise (scaling exponent = 0.5). This finding shows that the fractal dynamics of EEG rhythm is less random and more correlated in depressed patients than in controls. As a consequence, fractal analysis of resting EEG may be useful in understanding of brain neurodynamics in depression.

Summary:

Objectives : The development of fractal analysis has provided useful tools in the study of physiological systems. To search for a correlation between alterations in chaotic brain states and depressive disorders, we compared the fractal analysis of resting EEG signal in depressed patients to a control group of healthy adult.

Methods : The subjects in this study were 11 non-depressed, age matched controls, and in 14 un-medicated depressed patients. To classified as depressed, two criteria were imposed: (1) Beck Depression Inventory score of $\geq$ 10; and (2) A DSM-IV interview resulting in a diagnosis of depression. EEG data were obtained from each participant during five minutes resting baseline periods with eyes closed. Electrodes were placed at sites F3, F4, C3, C4, T3, T4, O1 and O2. To compare chaotic brain states with fractal analysis, we performed detrended fluctuation analysis (DFA), a well-established fractal analysis technique. The scaling exponent at each channel of each subject was statistically analyzed, which is the result of DFA. We used pared t-test to determine if there are any differences between the means of two groups.

Results : The following results were obtained. 1) All of the scaling exponents in depressed patients (0.92 ± 0.12) were greater than controls (0.81 ± 0.12). 3) In addition, significant differences for scaling exponents were found between patients and controls at sites F3, C3, C4, and T4 ($P<0.05$).

Conclusion : These results suggest that depressed patients have alterations in chaotic brain states. While the scaling exponents in patients were closer to 1/f noise (scaling exponent = 1), controls were closer to white noise (scaling exponent = 0.5). This finding shows that the fractal dynamics of EEG rhythm is less random and more correlated in depressed patients than in controls. Fractal analysis of resting EEG may be useful in understanding of brain neurodynamics in depression.

References:

1. Peng CK, Havlin S, Stanley HE, Goldberger AL. Quantification of scaling exponents and crossover phenomena in nonstationary heartbeat time series. Chaos 1995;5:82-87.
2. Lee JM, Kim DJ, Kim IY, Park KS, Kim SI. Nonlinear-analysis of human sleep EEG using detrended fluctuation analysis. Medical Engineering & Physics 2004;26:773-776.

NR542 Tuesday, May 23, 3:00 PM - 5:00 PM

Effects of Topiramate on Glucose Transport Via AMPK-Mediated Pathway in Rat L6 Skeletal Muscle Cells

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that topiramate increases glucose transport via AMPK-mediated pathway in rat L6 skeletal muscle cells.

Summary:

Body of evidence indicates anti-obesity and plasma glucose lowering effects of topiramate, a structurally novel anticonvulsant. Topiramate is also currently under going phase III trial as an anti-obesity agent. However, the mechanism of the action of topiramate has not been yet elucidated. In the present study we examined glucose transport by topiramate in L6 rat skeletal muscle cells. We first investigated the effect of topiramat on glucose uptake in L6 rat skeletal muscle cells. To further elucidate underlying mechanism, we studied AMP-activated protein kinase (AMPK) and insulin mediated pathways. Phospho-AMPK and p-p38 levels were assessed by Western blotting analysis. The contribution of AMPK to the effects of topiramate on glucose transport was examined either by its overexpression or by inhibition using wild-type or dominant-negative constructs. Glucose transport in L6 cells treated with topiramate was increased up to 2 fold, which is comparable to that with insulin treatment. The increased glucose transport was dose-independent. Pretreatment of LY294002, a PI3K inhibitor, exerted no effect on topiramate stimulated glucose transport while that of SB239063, p38 MAPK inhibitor, inhibited topiramate stimulated glucose transport to basal level. Phosphorylations of AMPK and p38 were increased. Dominant-negative AMPK abolished the enhancement of glucose transport by topiramate. Topiramate stimulates glucose transport via AMPK-mediated pathway in rat L6 skeletal muscle cells, further contributing to its potential anti-obesity and glycemic control properties and opening new perspectives for the possible new therapeutic agent.

References:

1. Roy Chengappa KN, Levine J, Rathore D, Parepally H, Atzert R: Long-term effects of topiramate on bipolar mood instability, weight change and glycemic control: a case-series. Eur Psychiatry 2001; 16: 186'190.
2. Woods TM, Eichner SF, Franks AS: Weight gain mitigation with topiramate in mood disorders. Ann Pharmacother 2004 May;38(5): 887-91.

NR543 Tuesday, May 23, 3:00 PM - 5:00 PM

Genetic Analysis of Glutathione *S*-Transferase (GSTM1 and GSTT1) Gene in Autism, Alcoholism, Schizophrenia, and Bipolar Disorder in Korean Population

Sang-Min Lee *Kyunghee Univ. Hospital, Psychiatry, # 1 Hoegi-dong, Dongdaemoon-gu, SEOUL, 130-702, Republic of Korea*, Geon-Ho Bahn, Ji-Young Song, Hwan-Il Chang, Long-Tai Zheng, Kyung-Kyu Lee, Jong-Woo Kim

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that a high likelihood of *GSTM1* and *GSTT1* null genotypes as a risk factor to the development of autism and alcoholism in Korean population.

Summary:

The glutathione S-transferases (GSTs) are a family of phase II conjugating enzymes that plays a crucial role in protecting cells from endogenous and exogenous electrophiles or reactive oxygen species. Oxidative stress-mediated cellular toxicity plays an important role in the pathophysiology of psychiatric disorders.

To determine whether *GSTM1* and *GSTT1* null polymorphisms were susceptible to the development of autism, we tested 233 autism and 1070 healthy controls. In addition, patients with other psychiatric disorders (143 alcoholism, 222 schizophrenia, and 69 bipolar disorder) were analyzed. The genetic analysis for the *GSTM1* and *GSTT1* polymorphisms was determined using multiplex polymerase chain reaction(PCR) approach. All data were analyzed with the statistical analysis software(SAS, version 8.2).

Frequencies of *GSTM1* and *GSTT1* nulls were significantly higher in autism than in controls (*GSTM1* null *vs* controls, 60.5% *vs* 47.0%; *GSTT1* null *vs* controls, 60.1% *vs* 48.0%), implicating *GSTM1* and *GSTT1* null genotypes may play a role in regard to autism ($P = 0.016$ for *GSTM1*, $P < 0.001$ for *GSTT1*). Given the odds ratio (OR) of *GSTM1* present/*GSTT1* present (+/+) was 1.00, the OR of *GSTM1* null/*GSTT1* null (-/-) was 2.48 (95% confidence interval (CI) = 1.53-4.03). We found a significant difference in *GSTM1* polymorphism, not in *GSTT1* polymorphism, between alcoholism and controls ($P = 0.007$, OR = 1.65, 95% CI = 1.14-2.37). As is the case with autism, *GSTM1*/*GSTT1* "double null" genotype was significantly associated with alcoholism and the OR was 2.43 (95% CI = 1.39-4.26) with both *GSTM1* and *GSTT1* absent (-/-). No difference in *GSTM1* or *GSTT1* polymorphism was observed in patients with schizophrenia or bipolar disorder.

In conclusion, our results suggest a high likelihood of *GSTM1* and *GSTT1* null genotypes as a risk factor to the development of autism and alcoholism in Korean population.

References:

1. Prabakaran S et al.: Mitochondrial dysfunction in schizophrenia: evidence for compromised brain metabolism and oxidative stress. Mol Psychiatry 2004; 9: 684-697.
2. Stroombergen MC, Waring RH: Determination of glutathione S-transferase mu and theta polymorphisms in neurological disease. Hum Exp Toxicol 1999; 18: 141-145.

NR544 Tuesday, May 23, 3:00 PM - 5:00 PM

Venlafaxine and Paroxetine are Both Effective for Hot Flashes in Menopausal Oriental Women

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Educational Objectives:

antidepressant use in hot flashes of menopause

Summary:

Background: Standard therapy for hot flash has been hormone therapy (HT). However, there were increased risks of adverse effect in a recent prospective study conducted by Women's Health Initiative. Recent data suggest that antidepressant may also be effective. However, there is no data in Asian patients. We conducted a single-blind, randomized trail to assess the efficacy on Taiwanese menopausal women.

Method: Patients recruited to the study were menopausal women suffering troublesome hot flash. Participants were assigned venlafaxine 75 mg (n=13), 150 mg (n=9), or paroxetine 20 mg daily (n=9). At baseline, these women received blood test, including estrogen and FSH and MINI interview. Study visits were scheduled for 1, 2, 4, and 8 weeks. Assessment tools included Daily hot flash diaries, and HAMD rating scale. Main outcome measures were mean change from baseline to week 8 in the visual analog scle of daily hot flash diaries.

Result: A total of 31 subjects with an average age of 49.4 ± 5.2 were enrolled. The mean BMI (body mass index) was 23.6 ± 3.2. 83% had psychiatric diagnosis by MINI and 17% didn't. 24 patients had evaluable data for the whole study period (10 group A, 8 group B, 6 group C). After 8 weeks, among group A: 90.0% got improved in hot flash score; group B: 100.0%,and among group C: 83.3%. No statistically significance between 3 groups. The mean reductions in hot flash score from baseline to week 8 were 53.3 ± 69.4 % by LOFC. The mean reductions were 74.2 ±27.2 % among patients with improvement. No statistical significance between improvements of hot flash and characteristics of these women, including age, BMI, psychiatric diagnosis, the score of HAMD, and estrogen and FSH levl.

Conclusion: Both antidepressants are effective in treating hot flash independent to psychiatric and depression severity.

References:

1. Stearrns V: paroxetine CR in the treatment of menopausal hot flashes. JAMA 2003; 289:2827-2835.
2. Kockler DR: Antidepressants as a treatment for hot flashes in women. Am J Health-Syst Pharm 2004; 61:287-292.

NR545 Tuesday, May 23, 3:00 PM - 5:00 PM

An Analysis of Common Endophenotypic and Genetic Characteristics of Negative Symptom Spectrum Disorders--Autism, Asperger's Disorder, and Schizophrenia: A Proposed Model for Genetic Investigation for Linking Candidate Gene Polymorphisms to Common Endophenotypes Across Different Disorders

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Educational Objectives:

At the end of this presentation, the participant should:

1. Understand the theoretical concept of negative symptom disorders
2. Recognize the overlap of certain endophenotypic features in autism and schizophrenia
3. Be aware of specific gene markers that have significant linkage disequilibrium across the disorders of autism, Asperger's syndrome, and schizophrenia
4. Appreciate the need for increased genome mapping, particularly as it relates to cross-disorder endophenotyping of specific symptoms.

Summary:

Abstract

Although the psychiatric literature to date has referred to "negative symptoms" almost exclusively within the context of schizophrenia, there seem to be a number of similar social deficits and cognitive/behavioral stereotypies in autism, Asperger's disorder, schizoid personality disorder, and schizotypal personality disorder as well. With the working hypothesis that these disorders may have overlapping genetic diatheses that could contribute to overlapping endophenotypes, we first systematically compared the DSM-IV diagnostic criteria for the different diagnoses to identify common endophenotypes. The results indicated that all of the disorders present with receptive and expressive deficits of emotion in social context as well as cognitive and behavioral stereotypies. Furthermore, they present in familial patterns, strongly suggesting a genetic cause or predisposition. A review of the literature indicated substantial information was available for genetic markers in schizophrenia, autism, and Asperger's disorder, but not for schizoid and schitzotypal personality disorders. We mapped all of the gene markers that had been reported to have significant linkage disequilibrium across the three disorders and found multiple regions that suggested overlap (Xp22.33, Xq13,11q21-22, 3q25-27, 3p14-21, 4p15, 4q31, 6q16, 7q31, and 13q14-21). The results for the X chromosome are particularly intriguing in light of the male predominance of Asperger's and autism as compared to schizophrenia. More in depth information is needed since all of the studies classified linkage disequilibrium with the disorders as a whole and not by their endophenotypes. The results in sum suggest that cross-disorder endophenotyping of specific symptoms should receive more emphasis in whole genome mapping work to identify particular regions of the genome that may be associated across different disorders with common endophenotypic symptomatology. The goal of this work was to propose a new technique for identifying potential susceptibility and protective genetic loci for disorders with similar endophenotypes to use as diagnostic and therapeutic targets.

References:

1. Hovatta I: Linkage analysis of putative schizophrenia gene candidate regions on chromosomes 3p, 5q, 6p, 8p, 20p and 22q in a population-based sampled Finnish family set. Mol Psychiatry 1998; 3(5):452-457.
2. Tentler D: A candidate region for Asperger syndrome defined by two 17p breakpoints. Eur J Hum Genet 2003; 11(2):189-195.

NR546 Tuesday, May 23, 3:00 PM - 5:00 PM

Paroxetine Versus Venlafaxine in the Relapse Prevention for Mmajor Depressive Disorder Among Han Chinese Population Living in Taiwan

Yi-Syuan Wu, B.S. *Tainan*, Yi-Chyan Chen, M.D., Ru-Band Lu, Prof. Dr.

Educational Objectives:

This report presents the results of an analysis of remission rates comparing lower dose of venlafaxine and paroxetine from 103 patitents with depression in Han Chinese population, which can serve as a reference to

the pharmacotherapeutic intervention in the clinical environment. At the conclusion of this presentation, the participants should take the doses of medication and the cut-off score on Hamilton Rating Scale for Depression used to define remission into account when comparing the efficacy of antidepressants.

Summary:

Introduction

Clinical studies suggested that venlafaxine had a rapid onset of action, producing significant clinical improvement in the first or

second week of treatment, and superior remission rate compared with paroxetine. However, few studies evaluated the relapse episodes in the 6-month continuation phase of treatment, and the cut-off score of the Hamilton Depression Rating Scale for Depression (HRSD) most frequently used to define remission was too high, which may be associated with lower rates of no psychosocial impairment. Thus the present, prospective 6-month study was carried out to investigate the efficacy, response and remission rate, to evaluate the prevention of relapse by continuation treatment with venlafaxine extended release (XR) or paroxetine.

Methods

This was a single center, open-label study of comparing venlafaxine XR and paroxetine on major depressive patients. Outpatients satisfying DSM-IV criteria for major depression with a baseline $HRSD_{17}$ score of at lease 16 were eligible. Following baseline evaluations, patients were assigned to treatment with venlafaxine XR 75 mg/day or 150 mg/day, or paroxetine 20mg/day for 6 months. The primary efficacy variables were the 6-month on-therapy total scores from the $HRSD_{17}$ scale and the remission rates ($HRSD_{17}$ score≤5), which were compared between treatment arms.

Results

103 patients, 50 treated with venlafaxine XR and 53 with paroxetine, were evaluated for efficacy. In pairwise comparisons, paroxetine was significantly superior ($p < .05$) to venlafaxine XR on the $HRSD_{17}$ at weeks 12, 16 and 24. After 24 weeks of treatment, the paroxetine group demonstrated a significantly higher remission rate than the venlafaxine XR group. Remission rates were: at week 24, venlafaxine XR, 12%(6/50), paroxetine, 32.1%(17/53) ($p<.05$).

Conclusions

Results suggest Paroxetine may be more effective than venlafaxine XR for treating outpatients with major depression in this 6-month study period. Based on remission criteria ($HRSD_{17}$ score≤5), paroxetine may be superior to venlafaxine XR.

References:

1. Thase ME, Entsuah AR, Rudolph RL: Rmission rates during treatment with venlafaxine or selective serotonin reuptake inhibitors. Br J Psychiatry 2001; 178:234-241.
2. Zimmerman M, Posternak MA, Chelminski I: Implications of using different cut-offs on symptom severity scales to define remission from depression. Int Clin Psychopharmacol 2004; 19:215-220.

NR547 Tuesday, May 23, 3:00 PM - 5:00 PM

Analysis of Remission in a Six-Month Double-Blind Continuation Study of Ziprasidone Versus Olanzapine

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Educational Objectives:

To emphasize the importance of using remission as a clinically relevant outcome variable, and to assess remission rates in a long-term trial of ziprasidone and olanzapine in patients with schizophrenia.

Summary:

Objective: To assess remission rates in a long-term, double-blind trial of ziprasidone and olanzapine in patients with schizophrenia.

Methods: Data were obtained from a 6 month, double-blind continuation trial of olanzapine and ziprasidone in the treatment of schizophrenia.[1] Criteria proposed by the Remission in Schizophrenia Working Group[2] (scores of 3 or less on items P1, P2, P3, N1, N4, N6, G5 and G9 of the PANSS) were used in this analysis.

Results: At continuation study baseline, remission rates (using severity criteria) were 60.7% and 59.1%, respectively, for the ziprasidone (n=56) and olanzapine groups (n=66). Remission rates using PANSS severity criteria were 64% (16/25) and 50% (14/28) (P=NS) for ziprasidone and olanzapine, respectively. Mean daily doses were 135.2 mg and 12.6 mg for ziprasidone and olanzapine, respectively.

Conclusions: Remission was achieved in a majority of patients in this post hoc analysis of remission rates (using PANSS severity criteria) at 6-months in a double-blind continuation trial of ziprasidone versus olanzapine.

References:

1. Simpson GM, Weiden P, Pigott T, et al: Six-month, blinded, multicenter continuation study of ziprasidone versus olanzapine in schizophrenia. Am J Psychiatry. 2005;162:1535-1538.
2. Andreasen NC, Carpenter WT Jr, Kane JM, et al: Remission in schizophrenia: proposed criteria and rationale for consensus. Am J Psychiatry. 2005;162:441-449.

NR548 Tuesday, May 23, 3:00 PM - 5:00 PM

A Randomized, Double-Blind, Placebo-Controlled, Flexible-Dose, Trial of Augmentation With OROS Methylphenidate in Treatment Resistant Depression

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Educational Objectives:

To understand the role of stimulant augmentation in the treatment of patients with major depression who have not responded or failed to respond to antidepressants.

Summary:

ABSTRACT BODY:

Objective: In the first randomized double-blind, placebo-controlled trial (RCT) of stimulant augmentation in Treatment Resistant Depression (TRD), we examined the efficacy and safety of augmenting with OROS methylphenidate (MPH) for non or partial responders to antidepressants

Methods: 60 subjects with TRD were enrolled in a 4-week RCT of OROS MPH (18 mg to 54 mg per day). The preexisting antidepressant dose was kept unchanged. The primary efficacy measure was a change in scores on the Hamilton Depression Rating Scale-21 item (HAM-D) from randomization to end of treatment. Secondary efficacy measures included changes in Clinical Global Impression- Improvement (CGI-I) and severity (CGI-S). Treatment response was defined as a ≥50% reduction in HAM-D or end of treatment CGI-I of 1 or 2. Results: 83% of subjects completed the study. The mean dose of methylphenidate Extended Release was 34.2 mg/day. ITT analyses found no statistically significant differences between OROS MPH (n=30) and placebo (n=30) in reduction in HAM-D (-6.9 in drug and -4.7 in placebo). ($F(1,47)=1.24$, $p=.22$). Although there were numerically more responders in the drug (40% by HAM-D, 43.3% by CGI-I) versus the placebo group (23.3% by HAM-D, 26.6% by CGI-I), this did not reach statistical significance. OROS MPH was well tolerated.

References:

1. Masand PS, Anand VS, Tanquary JF: Psychostimulant augmentation of second generation antidepressants. Depression and Anxiety 1997; 6:42-45.
2. Fava M, Thase M, DeBattista C: A multi-center, placebo-controlled study of modafinil augmentation in partial responders

to selective serotonin reuptake inhibitors with persistent fatigue and sleepiness. J Clin Psychiatry 2005; 66:85-93.

NR549 Tuesday, May 23, 3:00 PM - 5:00 PM

The Combination of Aripiprazole and Antidepressants in Psychotic Major Depression

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Educational Objectives:

At the conclusion of this presentation, the participant should be knowledgeable about the efficacy and tolerability of aripriprazole and escitalopram combination treatment for psychotic major depressive disorder.

Summary:

Abstract

Background: Although atypical antipsychotic agents are commonly used in the treatment of psychotic depression, there are few published prospective studies on their use in this condition. The aim of this study was to assess, by interim analyses, the efficacy of the atypical antipsychotic agent aripiprazole in combination with the escitalopram.

Methods: We enrolled 21 patients [ten (47.6%) women and eleven (52.4%) men] with MDD with psychotic features into an open trial of aripiprazole 5-30mg/day plus escitalopram 10-20mg/day. Patients were assessed at each visit with the HAM-D-17 and both the psychotic and mood modules of the SCID I/P. Responses were defined as: 1) absence of psychotic symptoms with 50% or greater reduction in HAM-D-17 scores (**Psychotic Depression Response**) and 2) the absence of psychotic symptoms as determined by the SCID psychosis module and a depression rating on the HAM-D-17 of less than 8 (**Psychotic depression remission**). We are reporting the results of the first eight weeks of treatment.

Results: Of the 21 enrolled patients, 11 of these patients [four (36.4%) women and seven (63.6%) men; mean age: 41.7 + 14.5] completed the 8-week open trial. Of the completers, 78.6% met criteria for melancholic features; 85.7% had delusions alone; 0.0% had hallucinations alone; and 100% reported both delusions and hallucinations. In addition, the completers showed a Psychotic Depression Response rate of 72.7%, and a Psychotic Depression Remission rate of 63.6%. Out of the 21 patients enrolled, 10 (47%) patients dropped out prior to completion; 2 (20%) of these drop-outs were due to intolerable side effects. In addition, the authors will review the side effect profile, metabolic changes and any serious adverse events.

Conclusion: The combination of aripiprazole plus escitalopram appears to be a promising, safe, and effective treatment for psychotic depression. Double-blind studies are needed to confirm this impression.

References:

1. Kane JM, Carson WH, Saha AR, McQuade RF, Ingenito GG, Zimbroff DL, Ali MW: Efficacy and safety of aripiprazole and haloperidol versus placebo in patients with schizophrenia and schizoaffective disorder. J Clin Psychiatry 2002; 63(9):763-771.

2. Matthews JD, Bottonari KA, Polania L, Mischoulon D, Dording CM, Irvin R, Fava, M: An.

NR550 Tuesday, May 23, 3:00 PM - 5:00 PM

Bioavailable Testosterone Levels and Its Association With Depression I Middle-Aged Men

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Educational Objectives:

To evaluate different indices of testosterone function in middle-aged men

To assess and compare measures of bioavailable levels of bioavailable testosterone in two groups of middle-aged men: currently depressed meeting DSM-IV-TR-defined criteria for Major Depressive Disorder and healthy controls.

Summary:

Background: The association between total testosterone levels (T) and depressive symptoms is variably reported. Bioavailable testosterone (BT) is the physiologically active moiety which hitherto has not been the primary dependent variable of interest in clinically depressed samples.

Methods: We cross-sectionally assessed and compared measures of BT levels in two groups of middle-aged men (40-65 years); currently depressed meeting DSM-IV-TR-defined criteria for MDD (N=44) and healthy controls (N=50).

Results: Depressed men had lower BT levels when compared to healthy controls (3.51+1.69 nmol/L and 4.69+2.04 nmol/L, respectively; $p<0.001$). Depressed men also had significantly lower T levels (11.94+4.63 nmol/L and 17.64+1.02 nmol/L; $p<0.001$). Biochemical hypogonadism (BT level<2.4nmol/L) was significantly more prevalent in the depressed men versus healthy controls (34% and 6%; $p<0.001$). Biochemical hypogonadism was associated with decrements in overall sexual satisfaction and desire in the full analysis set.

Conclusion: Bioavailable testosterone may be causal to the testosterone-depression association.

References:

1. Shores MM, Sloan KL, Matsumoto AM, Moceri VM, Felker B, Kivlahan DR: Increased incidence of diagnosed depressive illness in hypogonadal older men. Arch Gen Psychiatry 2004; 61(2):162-167.

2. Barrett-Connor E, Von Muhlen DG, Kritz-Silverstein D: Bioavailable testosterone and depressed mood in older men: the Rancho Bernardo Study. J Clin Endocrinol Metab 1999; 84(2):573-577.

NR551 Tuesday, May 23, 3:00 PM - 5:00 PM

Antidepressant Effectiveness in Primary-Care Settings

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Educational Objectives:

To evaluate antidepressant pharmacotherapy options and dosages in primary care-settings in Canada.

To compare the effectiveness of SSRIs and venlafaxine in the treatment of major depressive disorder (MDD) in naturalistic primary-care settings.

Summary:

Background: Describe and compare the effectiveness of SSRIs and venlafaxine (Effexor XR®) in the treatment of MDD in primary-care.

Method: Post-hoc analysis of data from a cross-national depression study conducted in primary care settings (n=47). Patients (n=143) completed 8-weeks of open-label SSRI or venlafaxine therapy. Patients with psychiatric and medical comorbidity were included as were concomitant medications. Both depression-specific (17-item Hamilton Depression Rating Scale, HAMD-17) and global measures (Clinical Global Impression - Improvement/Severity, CGI-I/S) were used to determine antidepressant effectiveness. Response to antidepressant treatment was defined as > 50% reduction in depression severity; remission was defined as a HAMD-17 score < 7.

Results: Depressed patients reporting to their primary-care provider were moderately depressed (HAMD-17: 23.2 +/- 4.3) at the initial visit prior to treatment initiation with either an SSRI (n=79) or venlafaxine (n=64). The reduction from baseline to week 8 in the total HAMD-17 score was significant for both groups (p<0.001) with no between-group differences (p=0.735). The response (SSRIs 77.2%, venlafaxine 82.8%, p=0.531) and remission (SSRIs 58.2%, venlafaxine 48.4%, p=0.312) rates were similar without any statistically significant difference between groups in time to response (p=0.890), remission (p=0.165), or global outcomes (CGI-I p=0.487, CGI-S p=0.821).

Conclusion: These data suggest that in nonselective, heterogenous, depressed, primary-care patients there is no apparent difference between SSRIs and venlfaxine in the probability of achieving remission. These descriptive data provide the impetus for a sufficiently powered study with comparable dosing.

References:

1. Rost K, Nutting P, Smith JL, Elliott CE, Dickinson M: Managing depression as a chronic disease: a randomised trial of ongoing treatment in primary care. BMJ 2002; 325(7370):934.
2. Thase ME, Entsuah AR, Rudolph RL: Remission rates during treatment with venlafaxine or selective serotonin reuptake inhibitors. Br J Psychiatry 2001; 178234-241.

NR552 Tuesday, May 23, 3:00 PM - 5:00 PM

Venlafaxine-Mirtazapine Combination in Persistent Depressive Illness

David J. Meagher *Regional Hospital, Dooradoyle, Limerick, Ireland*, Zaf Hamzah, Noel Hannan, Henry Akinpeloye

Educational Objectives:

To describe experiences during a naturalistic study involving the use of the novel antidepressant combination of venlafaxine and mirtazapine.

Summary:

Background: The combination of mirtazapine and venlafaxine has been suggested as a treatment option for difficult to treat depressive illness. We describe a series of patients with persistent depressive illness that received this combination therapy.

Method : Patients were identified by a prescribing audit. A retrospective review of these cases allowed for the assessment of doses used, clinical response on the CGI-improvement scale, and occurrence of adverse events.

Results : 32 patients [44% male; mean age 42 years; mean 2.5 previous antidepressant trials] had received mirtazapine and venlafaxine in combination at some point over the three year period between 2002 and 2005. Clinical response rates (CGI-improvement score of 2 or less) were 44% at four weeks and 50% at eight weeks. At six month review 75% of those still receiving treatment (n=24) had significantly responded. Clinical response typically occurred at moderate and high dose treatment with both agents. 44% experienced some adverse effects with sedation (19%) and weight gain (19%) most frequent. Five patients discontinued treatment due to these effects. No serious adverse effects were linked to the combination treatment.

Conclusions : The combination of venlafaxine and mirtazapine may be a useful therapeutic option in more difficult to treat patients. Our experiences suggest that this combination is safe and generally well tolerated.

References:

1. Carpenter LL, Yasmin S, Price LH (2002). A double-blind, placebo-controlled study of antidepressant augmentation with Mirtazapine. Biol Psychiatry 51:183-188.
2. Aydemir O, Taskin EO, Deveci A (2005). Mirtazapine augmentation in treatment-resistant major depressive disorder: an open-label, six week trial. European Neuropsychopharmacology 15;Suppl 3: 401-2.

NR553 Tuesday, May 23, 3:00 PM - 5:00 PM

Brain Structural Correlation of OCD and Depression Comorbidity

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Educational Objectives:

At the conclusion of this presentation the participant should be able to better understand some issues about the obsessive compulsive disorder (OCD) neurobiological substrate and the relationships with major depression (MDD). OCD and MDD comorbidity is a frequent situation with important clinical and therapeutic consequences. The knowledge of neuroestructural correlates of this comorbidity could allow deep inside the etiopathogeny of both disorders and to develop new diagnostic and treatment methods and strategies.

Summary:

Brain structural correlation of OCD and depression comorbidity

Background: The frequent comorbidity between OCD and major depression suggests a common neurobiological substrate. The aim of our study is to assess life-time depression contribution to structural brain alterations in OCD patients and to detect other comorbidity-related neurostructural correlations.

Methods: A sample of 39 outpatients with OCD, 33 outpatients with OCD and depression and 72 healthy control subjects were assessed with tridimensional MRI. Images were acquired with a 1.5-T MRI scanner, spatially normalized, and segmented with optimized VBM. Statistical comparisons were performed with the general linear model

Results: In a large sample of OCD patients lifetime depression was related to gray matter volume reduction in medial orfitofrontal cortex. An inverse correlation between medial OFC and right amygdala was found in OCD depressed patients. In addition OCD depressed patients lost the positive correlation between medial OFC and anterior cingulate cortex detected in non depressed OCD patients and healthy controls.

Conclusions: These findings suggest that life time depression may independently contribute to OCD brain estructural alterations, and are consistent with previous studies suggesting that alterations in amygdala and medial prefrontal cortex connectivity plays a critical role in diathesis for mood disorders .

References:

1. Pujol J, Soriano-Mas C, Alonso P, Cardoner N, Menchón JM, Deus J, Vallejo J. . Mapping structural brain alterations in ob-

sessive-compulsive disorder. Arch Gen Psychiatry 2004; 61(7): 720-730.

2. Saxena S, Brody AL, Ho ML, Alborzian S, Maidment KM, Zohrabi N et al. Differential cerebral metabolic changes with paroxetine treatment of obsessive-compulsive disorder versus major depression. Arch Gen Psychiatry 2002, 59(3): 250-261.

NR554 Tuesday, May 23, 3:00 PM - 5:00 PM

Comparative Effects of Ziprasidone and Olanzapine on Markers of Insulin Resistance: Results of a Six-Week Randomized Study in Patients With Acute Schizophrenia

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to:

1. Understand the use of biological markers associated with the development of insulin resistance
2. Appreciate the differential impact of olanzapine and ziprasidone on markers of insulin resistance

Summary:

Background: The ATP III criteria for metabolic syndrome have only 52% sensitivity for those in the upper tertile of insulin resistance, and fasting insulin achieves only 57% sensitivity, but a triglyceride:high density lipoprotein cholesterol (TG:HDL) ratio > 3.0 has 64% sensitivity.

Methods: Using data from a randomized, double-blind 6-week trial of ziprasidone versus olanzapine, analysis of TG:HDL ratio and other markers of insulin resistance was performed.

Results: At baseline, both drug cohorts had TG:HDL > 3 (ziprasidone 3.50±2.88, olanzapine 4.69±6.91). At endpoint, there was a significant increase in TG:HDL for the olanzapine-treated subjects (n=118) (5.99±7.37; p=.0001), but not for the ziprasidone cohort (n=110) (3.67±3.23; p=.435), and the between-group difference was significantly greater for olanzapine (p=.0062). The median change from baseline in fasting insulin was also significant for the olanzapine group (n=114) (3.30 μU/ml, p<.0001), but not ziprasidone (n=108) (0.25 μU/ml, p=0.33).

Discussion: TG:HDL ratio has been proposed as a sensitive marker of insulin resistance. In this short-term study, ziprasidone was associated with no significant change in TG:HDL ratio, in contrast to olanzapine which was associated with a significant increase in this parameter. Olanzapine treatment also significantly increased fasting insulin, while no significant effect was seen in the ziprasidone cohort. These findings are consistent with the ADA/APA Consensus Statement regarding the greater risk for diabetes and hyperlipidemia during olanzapine treatment relative to ziprasidone. Future research will help elucidate the mechanisms related to the differential liability for metabolic effects between atypical antipsychotics.

Support for this study was provided by Pfizer Inc.

References:

1. McLaughlin T, Abbasi F, Cheal K, Chu J, Lamendola C, Reaven G. Use of metabolic markers to identify overweight individuals who are insulin resistant. Annals of Internal Medicine 2003; 139(10):802-9.

2. Cheal KL, Abbasi F, Lamendola C, McLaughlin T, Reaven GM, Ford ES. Relationship to insulin resistance of the adult treatment panel III diagnostic criteria for identification of the metabolic syndrome. Diabetes 2004; 53(5):1195-200.

NR555 Tuesday, May 23, 3:00 PM - 5:00 PM

Chronobiological HPT Axis Dysfunction in Depression

Marie-Claude Mokrani, Ph.D. *Neurocom, Centre Hospitalier, Rouffach, 68250, France*, Fabrice Duval, M.D., Jose A. Monreal Ortiz, M.D., Christiane Champeval, Ph.D., Damien Maurice, Ph.D., Jean-Paul Macher, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand that the circadian chronesthesy (i.e. rhythmic change in the sensitivity of target biosystems) of pituitary TRH receptors is altered in depression. The reduced difference in TSH response between 11 PM and 8 AM TRH tests (ΔΔTSH), is a refined marker of this alteration.

Summary:

Background: The aim of this study was to evaluate the chronobiological hypothalamic-pituitary-thyroid (HTP) axis activity in depression. Method: Circadian rhythm of TSH, and TSH response to 8AM and 11PM TRH tests were determined in 141 drug-free DSM-IV major depressed inpatients, and 26 healthy hospitalized controls. Results: Circadian secretion of TSH showed a significant rhythm in controls and patients; however, mesor and amplitude were significantly lower in patients ($p<0.0005$ and $p<0.01$ respectively). According to their TRH-TSH test responses, patients were classified into 3 groups. Group 1 (n=41) had normal TSH responses; group 2 (n=35) had a reduced difference between 11 PM and 8AM responses (i.e. ΔΔTSH<2.5 mU/l), and group 3 (n=65) showed a reduced ΔΔTSH associated with a blunted TSH response at 11PM. The three groups showed a blunted surge of TSH (lower values than controls at 4 PM, 8 PM, midnight, 4 AM [all $p<0.01$]). However, the severity of this blunting was correlated with increased alterations of TRH-TSH responses. Conclusions: Our results suggest that the circadian chronesthesy of pituitary TRH receptors is altered in depression. One may hypothesize that this alteration is all the more pronounced since there is a prolonged increase in hypothalamic TRH stimulation.

References:

1. Duval F, Macher JP & Mokrani MC. Difference between evening and morning thyrotropin responses to protirelin in major depressive episode. Arch Gen Psychiatry 1990;47:443-448.

2. Duval F, Mokrani MC, Crocq MA, Jautz M, Bailey PE, Diep TS & Macher JP. Effect of antidepressant medication on morning and evening thyroid function tests during a major depressive episode. Arch Gen Psychiatry 1996;53:833-840.

NR556 Tuesday, May 23, 3:00 PM - 5:00 PM

Dopamine Dysregulation in Bipolar Depressed Patients

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand that dopamine (DA) dysfunction in bipolar depressed patients is not due to increased hypothalamic-pituitary-adrenal axis activity, but may reflect altered post-synaptic receptor sensitivity in the tuberoinfundibular DA system.

Summary:

Background: Indirect observations suggest that dopamine (DA) function may be altered in depressed patients, notably in bipolar

patients. The purpose of this study was to assess the DA receptor sensitivity at the hypothalamic-pituitary level in relation to the clinical course in depressed patients.

Method: We evaluated the multihormonal responses to the DA agonist apomorphine (APO, 0.75 mg SC) in 134 drug-free DSM-IV major depressed inpatients: 54 with bipolar depression (BD), 80 with unipolar depression (UD); compared with 36 healthy hospitalized controls (HCs). We also examined, in the same subjects, cortisol response to DST (DST, 1 mg orally).

Results: Responses to DST were comparable between UDs and BDs, although UDs had higher post-DST cortisol levels than HCs ($p < 0.05$). No significant difference in cortisol, adrenocorticotropin and growth hormone values was found (i.e. at baseline and in response to APO) across the 3 diagnostic groups. However, BDs had lower APO-induced PRL suppression than HCs and UDs (both $p < 0.00001$).

Conclusions: In bipolar depressed patients, blunted APO-induced PRL suppression may reflect altered D2 receptor sensitivity of the lactotrophs (possibly secondary to an increased tuberoinfundibular dopamine neuronal activity); this blunting does not appear to be linked to an increased hypothalamic-pituitary adrenal axis activity.

References:

1. Mokrani MC, Duval F, Crocq MA, Bailey P, Macher JP. Multihormonal responses to apomorphine in mental illness. Psychoneurendocrinology 1995;20:365-375.
2. Monreal JA, Duval F, Mokrani MC, Pinault G, Macher JP. Dopamine function in bipolar and unipolar depressed patients. Ann Med Psychologiques 2005;163:399-404.

NR557 Tuesday, May 23, 3:00 PM - 5:00 PM

Effects of Risperidone on Anterior Cingulate Cortex Glutamate in Pediatric Bipolar Disorder

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Educational Objectives:

At the conclusion of this presentation the participant should have an understanding of the possible mechanism of action of risperidone in pediatric bipolar disorder

Summary:

Studies have shown that atypical antipsychotics increase serum glutamate levels in subjects with schizophrenia. Proton MRS demonstrated that the atypical antipsychotic olanzapine increased the anterior cingulate cortex glutamate+glutamine to creatine ratio in schizophrenia. Atypical antipsychotics are used to treat BPD in children. While these medications are effective in treating children with BPD it is not clear what their mechanism(s) of action are. The purpose of this study was to investigate ACC Glx/Cr in two groups of children with BPD: those not receiving treatment with an antipsychotic and those being treated with the atypical antipsychotic risperidone

Proton MR spectra were acquired, at 1.5 T, from a 4.8 ml region in the ACC of 20 subjects with a DSM IV diagnosis of BPD: eight (10.88 ± 2.99 years; 1 female) were medicated with the atypical antipsychotic risperidone and twelve (11.42 ± 3.48 years; 6 female) were not medicated with an atypical antipsychotic

There was a significant positive effect of risperidone on Glx/Cr ($B= 0.34$, $t = 2.46$, $p < 0.03$) and a significant negative effect of YMRS on Glx/Cr ($B= -0.01$, $t = -2.99$, $p < 0.009$). Children treated with risperidone had significantly lower YMRS scores than children not treated with risperidone (32.3 ± 5.74 versus 7.86 ± 5.87; $df = (1, 16)$; $F = 73.37$; $p < 0.000$). There were no significant effects of age or sex on Glx/Cr.

The proton MRS Glx peak arises largely from glutamate. Risperidone may be acting in pediatric BPD by increasing brain glutamate levels. Reduced glial and neuronal density have been measured in the dorsolateral prefrontal cortex of subjects with BPD. Glia provide the major pathway for neuronal glutamate synthesis. Reduced glial function would account for reduced glutamate synthesis. A possible mechanism of action of risperidone may be to increase ACC glutamate levels.

NR558 Tuesday, May 23, 3:00 PM - 5:00 PM

Metabolic Screening in Patients Prescribed Atypical Antipsychotics

Charles D. Motsinger, M.D. *Malcolm Grow Medical Center, Family Practice and Psychiatry, 1075 W Perimeter Rd, Andrews AFB, MD, 20872*

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the low rate of screening for metabolic abnormalities in patients prescribed atypical antipsychotics. The participant should also understand the current guidelines for metabolic screening in patients prescribed atypical antipsychotics and be able to describe possible reasons for low compliance with these recommendations.

Summary:

Title: Metabolic Screening in Patients Prescribed Atypical Antipsychotics

Objective: The aim of this study was to determine the rate of screening for metabolic abnormalities in patients taking atypical antipsychotics.

Method: A pharmacy database review identified patients who were prescribed atypical antipsychotics over a six month period. This list of patients was then cross-referenced with the laboratory database to determine if screening laboratory tests for metabolic abnormalities had been ordered.

Results: 13% of patients prescribed atypical antipsychotics had fasting blood glucose measured during the study period. 30% of these patients also had lipid panels measured during the study period. Screening rates varied by specialty of physician. Physicians trained in Combined Family Practice-Psychiatry had the highest rate of screening, followed by other non-psychiatric specialties. Psychiatrists had the lowest rate of screening.

Conclusions: The rate of screening for metabolic side effects of atypical antipsychotics in this community hospital setting was low.

References:

1. American Diabetes Association, American Psychiatric Association, American.
2. Casey DE: Metabolic issues and cardiovascular disease in patients with psychiatric disorders. Am J Med 2005; 118 Suppl 2: 15S-22S.

NR559 Tuesday, May 23, 3:00 PM - 5:00 PM

Treatment With Venlafaxine XR or Placebo in Patients With PTSD Resilience as a Predictor of Remission

Jeff Musgnung *Wyeth Pharmaceuticals, 500 Arcola Road, Collegeville, PA, 19426*, Jonathan Davidson, M.D., Dan J. Stein, M.D., Barbara Rothbaum, Ph.D., Xiao Wei Tian, Ron Pedersen, M.S.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to: 1. Explain the importance of predictors of remission and response in the treatment of posttraumatic stress disorder. 2. Describe key outcome measures used in assessing remission and response in patients with posttraumatic stress disorder. 3. Evaluate resilience as a predictor of remission and response in patients with posttraumatic stress disorder treated with venlafaxine extended release or placebo.

Summary:

Objective: To evaluate resilience as a predictor of remission in posttraumatic stress disorder (PTSD) patients treated with venlafaxine (Effexor® extended release (XR) or placebo.

Methods: Data were evaluated from a 3-month study and a 6-month study of adult outpatients with a primary diagnosis of DSM-IV PTSD, PTSD symptoms for ≥6 months, and 17-item Clinician-Administered PTSD scale (CAPS-SX_{17}) score ≥60. Patients were randomly assigned to treatment with flexible-dose venlafaxine XR (37.5 to 300 mg/day) or placebo. In addition to the CAPS-SX_{17}, outcome measures in both studies included the Davidson Trauma Scale (DTS), Sheehan Disability Scale (SDS), and Connor-Davidson Resilience Scale (CD-RISC). Using last-observation-carried-forward values, baseline CD-RISC items predictive of remission (defined as CAPS-SX_{17} ≤20) were identified by logistic regression and baseline CD-RISC items predictive of response on the CAPS-SX_{17}, DTS, and SDS (defined as score change from baseline) were evaluated using multiple regression.

Results: For the 3-month study (venlafaxine XR, n=179; placebo, n=179), items 22 ('In control of your life') and 25 ('Pride in your achievements') were significant (P<0.05) predictors of remission. For the 6-month study (venlafaxine XR, n=161; placebo, n=168), items 7 ('Having to cope with stress can make me stronger') and 9 ('Good or bad, I believe that most things happen for a reason') were significant predictors. Items predicting CAPS, SDS and DTS response were also found, although the items predicting response differed between studies.

Discussion: A number of CD-RISC items significantly predicted remission and response on clinician- and self-ratings of PTSD, although predictors differed between studies.

References:

1. Connor KM, Davidson JR: Development of a new resilience scale: the Connor-Davidson Resilience Scale (CD-RISC). Depress Anxiety 2003; 18:76-82.

2. Davidson JR, Payne VM, Connor KM, Foa EB, Rothbaum BO, Hertzberg MA, Weisler RH: Trauma, resilience and saliostasis: effects of treatment in post-traumatic stress disorder. Int Clin Psychopharmacol 2005; 20:43-48.

NR560 Tuesday, May 23, 3:00 PM - 5:00 PM

Correlations Between Four Outcome Scales in Clinical Trials in Patients With Major Depressive Disorder

Jeff Musgnung *Wyeth Pharmaceuticals, 500 Arcola Road, Collegeville, PA, 19426*, Qin Jiang, Saeed Ahmed, Ron Pedersen, Richard Entsuah

Educational Objectives:

At the conclusion of this presentation, the participant should be able to:

1. Examine the relationship between 4 scales used to assess outcomes in major depressive disorder

2. Describe correlations between outcomes scales at different time points before and during antidepressant treatment

Summary:

Objective: Examine the relationship between the 17-item Hamilton Depression Rating Scale (HAM-D_{17}), the Montgomery-Asberg Depression Scale (MADRS), and the Clinical Global Impression of Severity (CGI-S) and CGI-Improvement (CGI-I) in patients with MDD.

Methods: Data from 22 randomized, double-blind, placebo-controlled venlafaxine (Effexor®) studies in patients with MDD were pooled and examined from baseline through the first 8 weeks of treatment. For all rating scales, Pearson Correlation coefficients were calculated for patients at each visit, between change scores, and by treatment arm. Correlations between binary outcomes (response defined as CGI-I and CGI-S ≤2, 50% decrease in HAM-D_{17} and MADRS) were determined.

Results: At pretreatment visits, for the HAM-D_{17}, MADRS, and CGI-S, respectively, 5117, 4871, 5103 observations were available, with mean scores of 23.0, 29.1, 4.4. Pretreatment correlations ranged from 0.52 (CGI-S and HAM-D_{17}), 0.53 (CGI-S and MADRS) and 0.62 ($HAMD_{17}$ and MADRS). Correlations between scales increased at each visit, and at 8 weeks, ranged from .87 (CGI-S and CGI-I) to .93 (HAM-$D_{17}$and MADRS). Correlation coefficients in treatment arm subgroup analyses and between change scores were comparable. Correlation coefficients between binary outcomes (response defined as CGI-I and CGI-S of 2 or less, 50% decrease in HAM-D and MADRS) were lower, ranging from .42 (CGI-I and CGI-S) to 0.61 (HAM-D_{17} and MADRS) at week 1 and from .61 (CGI-I and CGI-S) to 0.81 (HAM-D_{17} and MADRS) at week 8. All correlation coefficients were highly significant (P<.0001).

Conclusions: Correlations between the 4 commonly used outcome scales were high; however, correlations between binary outcomes based on the scales were lower. As they share several items and have similar modes of administration and rating, the highest correlations were between the HAM-D_{17} and the MADRS. Somewhat surprising were the modest but consistently lower correlations between the CGI-S and CGI-I scales, which are sometimes considered interchangeable.

References:

1. Mulder RT, Joyce PR, Frampton C: Relationships among measures of treatment outcome in depressed patients. J Affect Disord 2003; 75: 127-135.

2. Khan A, Brodhead AE, Kolts RL: Relative sensitivity of the Montgomery-Asberg depression rating, scale, the Hamilton depression rating scale and the Clinical Global Impressions rating scale in antidepressant clinical trials : a replication analysis. I.

NR561 Tuesday, May 23, 3:00 PM - 5:00 PM

Issues Related to Treatment Compliance in Bipolar Patients

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Educational Objectives:

Educational Objective: At the conclusion of this presentation, the participants will be able to understand issues related to treatment compliance in Bipolar Patients.

Summary:

Objective: There is limited data on treatment compliance in patients with Bipolar Disorder. We examined the characteristics of compliance in a large group (n=637) of bipolar patients to determine any significant relationships between compliance with treatment and demographic characteristics, types of medication used for treatment and length of time in treatment.

Methods: We extracted data on bipolar patients from a larger dataset of over 5,000 patients with Psychiatric Disorders. Treatment spanned a two-year period and the database contained information on the numbers, types, dose, and supplies of medications prescribed and filled by a pharmacist as well as diagnoses. Compliance was defined as the proportion of time in treatment *after* a diagnosis of bipolar disorder. Compliance categories were: 1) no compliance; 2) partial compliance: 1-5 months without a 30-day supply of medication; and 3) full compliance- the patient filled prescriptions for each month over the 2-year period. Seventy-seven percent were female and 23% were male. The average number of months in treatment was 19 months. The average time to a diagnosis of bipolar disorder was 12 months (6.77). Fifty-three percent of bipolar patients were fully compliant with treatment; 27 % were partially compliant; and 20% were not compliant. Bipolar patients, aged 18-25 years, were significantly less complaint compared to older patients (X^2= 37.8 (6); p=0.000). Patients were more compliant with treatment if they started medication during the same month as a bipolar diagnosis or were taking the atypical antipsychotic Resperidone. Patients were more likely to be compliant with treatment if they continued on their prescribed medications over the two-year period (for mood stabilizers: X^2= 42.7(10); p=0.000 and for antipsychotic mediations: X^2=22.88; p=0.011).

Conclusions: Some characteristics of treatment compliance for bipolar patients are older age, starting medication soon after a diagnosis and how long patients continued the prescribed medication.

References:

1. Weiden PJ et al Partial compliance and risk of rehospitalization among California Medicaid patients with Schizophrenia. Psychiatric Services 2004; 55:886-891.
2. Steiner JF et al The assessment of refill compliance using pharmacy records: methods, validity, and applications. J Clin Epidemiology 1997; 50:106-116.

NR562 Tuesday, May 23, 3:00 PM - 5:00 PM

Adjunctive Use of Low Dose Quetiapine in Affective Disorder Outpatients

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand that low doses of quetiapine can be effective as augmentation to other medications in the treatment of affective disorder patients.

Summary:

Objective: To determine the effectiveness of long term low doses of quetiapine in the adjunctive treatment of patients with affective disorders

Methods: A chart review was performed on all patients currently being seen in a private, rural, outpatient psychiatric office. Patients were included in the study if they were taking 200mg or less of quetiapine daily for 6 months or longer. Patient demographics, medication history, Carroll Depression Rating Scale (CDRS) scores, and Visual Analog Scale (VAS) scores were collected.

Results: 28 patients met the criteria of being on quetiapine for at least 6 months with a daily dosage of 200mg or less. There were 20 females, and 8 males. The average age was 56(±15.6). 24 patients had a clinical diagnosis of unipolar depression or bipolar depression, and 4 patients had other diagnoses . In all cases, quetiapine was used as an adjunct to other psychiatric medications, and was the only antipsychotic used. Patients were on an average of 2.0(±1.0) other medications. Patients were on an average daily dosage of 85mg(±57) for an average period of 2.7(±1.9) years. Their initial CDRS score was 16.4(±10.5). It decreased to 11.6 (±10.8) after 6 months (p<0.002 versus baseline), 11.2 (±9.8) after 1 year (p<0.02 versus baseline), and 11.6 (±11.7) after 2 years (p<0.03). The average final score was 10.4(±9.2) (p<0.001 versus baseline). 68% of these patients achieved remission as defined by a CDRS score of <7. The average initial VAS score was 3.71 (±1.9). It increased to 4.7 (±2.1) at 6 months (p<0.02 versus baseline), 4.6(±2.0) at 1 year (p<0.05), and 4.4(±1.8) after 2 years (p<0.05). The average final score was 5(±1.4) (p<0.01 versus baseline).

Conclusions: Low doses of quetiapine were shown to be effective and well tolerated as an augmentation of other medications in a group of affective disorder outpatients.

References:

1. Calabrese JR, Keck PE Jr, Macfadden W et al: A randomized, double-blind, placebo-controlled trial of quetiapine in the treatment of bipolar I or II depression. Am J Psychiatry 2005; 162:1351-60.
2. Sokolski KN, Denson TF: Adjunctive quetiapine in bipolar patients partially responsive to lithium or valproate. Prog Neuropsychopharmacol Biol Psychiatry 2003; 27:863-6.

NR563 Tuesday, May 23, 3:00 PM - 5:00 PM

Predictors of Switching Antipsychotics in the Treatment of Schizophrenia

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Educational Objectives:

At the conclusion of this presentation, the participant should recognize that switching of antipsychotics appears to be a prevalent phenomenon in the treatment of schizophrenia, and that one can use a small and distinct set of clinical measures to predict who is most likely to switch antipsychotics during the following year.

Summary:

Objectives: To identify which patient baseline characteristics and which types of early changes in patients' clinical status are most predictive of switching antipsychotics in the long-term treatment of schizophrenia.

Methods: This post-hoc analysis used data from a randomized, open-label, multi-site, one-year cost-effectiveness trial of olanzapine, risperidone, and typical antipsychotics in the treatment of schizophrenia. Study protocol permitted switching of antipsychotics when clinically warranted. Baseline characteristics were assessed using standard psychiatric measures and systematic review of medical records. In addition to baseline socio-demographics, co-morbid medical and psychiatric conditions, body weight, clinical, and functional characteristics, the prediction model included change scores on clinical measures (PANSS, five PANSS factor subscales, Barnes Akathisia Scale, Simpson Angus Scale) during the first 2 weeks of treatment. Cox proportional hazards model was used to identify the best predictors of switching from patients' initial randomized antipsychotic.

Results: About one-third (29.5%, 190/644) switched antipsychotics before the end of the one-year trial. Five variables were identified as best predictors of switching during the 1-year trial (p<.05): absence of antipsychotic use in the prior year, pre-existing depression, lack of lifetime substance use disorder, less improvement or worsening following 2 weeks of treatment on either clinician-rated akathisia (Barnes Akathisia Scale), and/or anxiety/depression symptoms (PANSS). A strong trend was observed for female gender (p=.058). **Conclusions:** Switching of antipsychot-

ics appears to be prevalent in the naturalistic treatment of schizophrenia, and can be predicted by a small and distinct set of measures. Interestingly, pre-existing depressive symptomatology and less improvement or worsening of anxiety and depressive symptoms following 2 weeks of treatment were among the more robust predictors of future switching of antipsychotics in this 1-year study.

References:

1. Tunis SL, Kinon BJ, Faries DE, Ascher-Svanum H, Nyhuis AW, Aquila R. Cost-Effectiveness of Olanzapine as First-Line Treatment for Schizophrenia: Results From a Randomized, Open-Label, One-Year Trial. Value in Health, in press.
2. Hugenholtz GW, Heerdink ER, Nolen WA, et al. Less medication switching after initial start with atypical antipsychotics. European Journal of Neuropsychopharmacology 2002;14:1-5.

NR564 Tuesday, May 23, 3:00 PM - 5:00 PM

Algorithms for the Psychopharmacology of Major Depression and Dysthymia: 2006 Update

David N. Osser, M.D. *Taunton State Hospital, 60 Hodges Avenue Extension, Taunton, MA, 02780*, Mathews Thomas, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to select evidence-supported, cost-effective pharmacotherapy for patients with major depression or dysthymia.

Summary:

Background:

This is a revised version of the web-based psychopharmacology algorithms for major depression (non-psychotic) and dysthymia of the Psychopharmacology Algorithm Project at the Harvard South Shore Psychiatry Department, currently available online at www.mhc.com/Algorithms. The website has won awards including the 2004 Lundbeck International Neuroscience Foundation Award for excellence in postgraduate education in psychiatry and neurology. In this revision, significant changes have been made to emphasize cost-effectiveness considerations in the sequence of clinical decisions.

Methods:

The authors evaluated the existing algorithms and associated texts for currency and accuracy. Evidence-based medicine searches were done to answer the clinical questions relevant to each algorithm node. Particular emphasis was placed on systematic critical reviews, and then randomized, controlled trials, observational studies, case reports, and compilations of expert consensus opinion. Other algorithms (e.g.- Texas Algorithm Project) were studied. Based on these reviews and cost tables, we determined if there was sufficient justification for changes in the sequence of recommendations. The revision was presented to local experts for comment.

Results:

SSRI's (generics preferred) and bupropion are still first-line options. Bupropion is much more costly but could be preferred if sexual side effects are a critical issue. Three sequential antidepressant monotherapy trials are proposed, even if there is partial response, since the cost-effectiveness of augmentation approaches is not demonstrably superior. ECT can be a first line option for high-risk patients. Augmentations are rated according to the quality of the evidence base, toxicity potential, and cost. For example, mirtazapine augmentation and atypical antipsychotic augmentation have similar evidence but toxicity and cost favor mirtazapine.

Conclusion:

This revision responds to the need for more financially responsible decision-making in the pharmacotherapy of depression while maintaining the algorithms' focus on treatment sequences that are reasonably safe and evidence-supported.

The Algorithm Project and authors receive no support from any pharmaceutical firms.

References:

1. Osser DN, Patterson RD: Algorithms for the pharmacotherapy of depression. Directions in Psychiatry 1998;18:303-334.
2. Parker GB, Malhi GS, Crawford JG, Thase ME: Identifying 'paradigm failures' contributing to treatment-resistant depression. J Affect Disord 2005;87:185-191.

NR565 Tuesday, May 23, 3:00 PM - 5:00 PM

Aripiprazole Augmentation for Patients With Major Depressive Disorder Who Failed to Respond to Antidepressant Therapy

Chi-Un Pae, M.D. *Duke University, Psychiatry and Behavioral Sciences, 4323 Ben Franklin Blvd., Suite 700, Durham, NC, 27704*, Ashwin Patkar, M.D., Andersson Candace, Ph.D., Chul Lee, M.D., In-Ho Paik, M.D., Prakash S. Masand, M.D.

Educational Objectives:

At the conclusion of this presentation, the participants should be able to understand the potential role of augmentation with atypical antipsychotics such as aripiprazole for patients with major depression who have failed to respond to therapeutic antidepressant therapy.

Summary:

Objectives: The present study evaluated whether augmentation with aripiprazole would be beneficial and tolerable in patients who failed to adequately respond to a therapeutic trial of antidepressants (ADs).

Methods: Thirteen patients with non-psychotic major depression who had failed to respond to an adequate trial of at least one antidepressant were prescribed open-label, aripiprazole (dose 5-30 mg/day) for 8 weeks. The dose of pre-existing antidepressants remained unchanged. Primary outcome measure was a change in Hamilton Depression Rating Scale (HAM-D) score from baseline to end of treatment. Treatment response was defined as 50% or greater reduction in HAM-D score from baseline to end of treatment.

Results: Eleven (84.6%) patients returned for at least one post follow up visit and 7 (53.8%) patients completed the study. The mean dose of aripiprazole was 10.8 $\pm$ 2.4 mg/d. The HAM-D (-14.1, 53.8% decrease) and Clinical Global Impression-severity (CGI)-S scores (-3.1, 56.0% decrease) reduced significantly from baseline to end of treatment ($Z=-2.937$, $p=0.003$; $Z=-2.961$, $p=0.003$). At end of treatment, 7(63.6%) patients showed 50% reduction or greater in HAMD score and 3 (27.3%) met the remission criteria. There were no serious adverse events. Three patients (23.1%) experienced mild tremor and/or akathisia.

Conclusions: Augmentation with aripiprazole appears to have clinical benefit in the treatment of depressed patients who show inadequate response to antidepressants. Given the limitations of an open-label design and small sample size, adequately powered, randomized, controlled trials are necessary to address this issue.

References:

1. Barbee JG, Conrad EJ, Jamhour NJ: Aripiprazole augmentation in treatment-resistant depression. Ann Clin Psychiatry 2004; 16:189-194.
2. Gupta S, Masand P: Aripiprazole: review of its pharmacology and therapeutic use in psychiatric disorders. Ann Clin Psychiatry 2004; 16:155-166.

NR566 Tuesday, May 23, 3:00 PM - 5:00 PM

Metabolic Syndrome and Metabolic Abnormalities in Patients on Second-Generation Antipsychotics: A Large-Scale Outpatient Sample

Osman M. Ali, M.D. *New York, NY*, Rachelle H. Ramos, M.D., Michelle S. Izmirly, D.O., Heather Morse, M.D., Karen Weinstein, Ph.D., Anand Pandya, M.D.

Educational Objectives:

By the end of this presentation, participants will be able to identify two specific and sensitive initial screening methods for metabolic syndrome.

By the end of this presentation participants will be aware of the prevalance of Metabolic Syndrome among psychiatric outpatients on second generation antipsychotic medications.

Summary:

Background: The estimates of prevalence of metabolic abnormalities in psychiatric patients vary widely[i,ii] and studies of Metabolic Syndrome (MetSynd) in patients on Second-Generation Antipsychotics (SGAs) tend to look at specific diagnostic groups rather than the full range of psychiatric patients that use these medications. We describe the prevalence of metabolic abnormalities and MetSynd in 426 psychiatric outpatients taking SGAs, a larger sample than previous studies. Method: Age, gender, height, weight, BMI, blood pressure, waist circumference, fasting glucose, and fasting lipids were obtained from subjects in a dozen programs including clinics, day treatment programs and residential programs. We compared those with and without MetSynd using chi-square tests for gender and using an analysis of variance for the other variables. We computed sensitivities, specificities and predictive values for diagnosing MetSynd using combinations of each component criteria. Results: 37.8% (161/426) met criteria for MetSynd. Waist circumference was the most sensitive single predictor of MetSynd (96.8 %). A combination of waist circumference, triglycerides and systolic blood pressure achieved 91.1% sensitivity and 100% specificity. Waist circumference with systolic blood pressure criteria also obtained 100% specificity. Discussions: Non-laboratory criteria may provide a sensitive and specific initial screening for MetSynd. Rates of MetSynd in all patients on SGAs are similar to previously published rates of MetSynd in Patients with Schizophrenia on SGAs.

References:

1. Daumit GL, Clark JM, Steinwachs DM, Graham CM, Lehman A, Ford DE. Prevalence and correlates of obesity in a community sample of individuals with severe and persistent mental illness. J Nerv Ment Dis. 2003; 191:799-805.
2. Straker D, Correll CU, Kramer-Ginsberg E, et al: Cost-effective screening for the metabolic syndrome in patients treated with second-generation antipsychotic medications. Am J Psychiatry. 2005;162:1217-1221.

NR567 Tuesday, May 23, 3:00 PM - 5:00 PM

A Meta-Analysis of Clinical Trials Comparing Mirtazapine With Selective Serotonin Reuptake Inhibitors for the Treatment of Major Depressive Disorder

George I. Papakostas, M.D. *Massachusetts General Hospital, Psychiatry, 15 Parkman Street, WACC 812, Boston, MA, 02114*, Maurizio Fava, M.D.

Educational Objectives:

At the end of this presentation, the participant should be able to cite potential differences in antidepressant efficacy when comparing mirtazapine with the SSRIs.

Summary:

Context: Over the past few years, a number of studies have suggested that the treatment of MDD with antidepressants enhancing both noradrenergic as well as serotonergic neurotransmission may result in higher response or remission rates than treatment with antidepressants selectively enhancing serotonergic neurotransmission.

Objective: The objective of this paper was to compare response rates among patients with MDD treated with either mirtazapine, an antidepressant thought to simultaneously enhance both noradrenergic and serotonergic neurotransmission, or SSRIs.

Data Sources: Medline/Pubmed were searched. No year of publication limits were used.

Study Selection: Double-blind, randomized clinical trials comparing mirtazapine with an SSRI for the treatment of MDD.

Data Extraction: Data were extracted with the use of a precoded form.

Data Synthesis: Analyses were performed comparing response rates between the two antidepressant agents. Data from 9 reports involving a total of 1882 outpatients with MDD were identified and combined using a random-effects model. Patients randomized to treatment with mirtazapine were as likely to experience clinical response as patients randomized to treatment with an SSRI (RR= 1.07; 95% CI: 0.95-1.2, p=0.227). There was no difference in overall discontinuation rates (RR=1.1; 95% CI: 0.7-1.5; p=0.550), discontinuation rates due to adverse events (RR= 0.9; 95% CI: 0.6-1.2; p=0.497), or discontinuation rates due to lack of efficacy (RR=0.9; 95% CI: 0.4-2.0; p=0.871) between the two groups. Fewer mirtazapine-treated patients complained of insomnia (RR=0.5; 95% CI: 0.3-0.9; p=0.017), while fewer SSRI-treated patients complained of fatigue (RR=1.5; 95% CI: 1.1-2.4 p=0.028) or excessive sleepiness (RR=1.3; 95% CI: 1.1-1.7; p= 0.020) during the course of treatment.

Conclusions: These results suggest that mirtazapine and the SSRIs differ with respect to their effects on sleep and fatigue, but not overall efficacy in the treatment of MDD.

References:

1. Smith D, Dempster C, Glanville J, Freemantle N, Anderson I. Efficacy and tolerability of venlafaxine compared with selective serotonin reuptake inhibitors and other antidepressants: a meta-analysis. Br J Psychiatry. 2002;180:396-404.
2. Quitkin FM, Taylor BP, Kremer C. Does mirtazapine have a more rapid onset than SSRIs? J Clin Psychiatry. 2001;62(5):358-61.

NR568 Tuesday, May 23, 3:00 PM - 5:00 PM

Pharmacogenetic Approach of Autism: Microarray Profile of Maternal Separation Animal Model and Association Study of Candidate Genes in Korean Autistic Patients

Jun-Heon Park, M.D. *College of Medicine, Kyung Hee University, Seoul, Korea, Department of Neuropsychiatry, Dept of psychiatry, KyungHee Univ.Hospital, #1 Hoegidong, Dongdaemoon-gu, Seoul, 130-702, Republic of Korea*, Sang-Min Lee, Hwan-Il Chang, Geon-Ho Bahn, Joo-Ho Chung, Kyung-Kyu Lee, Jong-Woo Kim

Educational Objectives:

At the conclusion of this presentaion, the participant should be able to know that among known 17 SNPs, only one polymorphism(Thr139Thr) of transthyretin gene showed heterozygosity in autistic spectrum disorder or healthy children. In addition,the haplotype of TPH 2 and PCLO was associated with autism in Korean population.

Summary:

Early maternal separation has been shown to produce enduring morphological changes in the hippocampus and other brain structures, and appear autistic behaviors. Furthermore, the early loss of maternal care may affect the vulnerability of the infant to neuropsychiatric disorders, such as childhood anxiety disorders, personality disorders and depression, over its lifespan.

In this study, rat pups were separated from their mothers and socially isolated on postnatal day 14-21. To identify the candidate genes in the hippocampus, 5.0k rat cDNA microarray analysis was performed with separated pups. In separated pups, four genes were up-regulated and two down-regulated at least 2-folds compared to non-separated pups (control). Next, genetic study of transthyretin gene selected from above results was carried out. Among known 17 SNPs, only one polymorphism (Thr139Thr) of transthyretin gene showed heterozygosity in autistic spectrum disorder or healthy children. Thr139Thr polymorphism in Korean autism was not associated. In addition, tryptophan hydroxylase (TPH) 2 and piccolo (PCLO) genes were analyzed. The haplotype of TPH 2 and PCLO was associated with autism in Korean population.

References:

1. Murcia CL, Gulden F, Herruo K : A question of balance: a proposal for new mouse models of autism. Int J Devl Neuroscience 23(2005) 265-275.

2. Chugani DC : Serotonin in autism and pediatric epilepsies. MRDD Research Reviews 10(2004) 112-116.

NR569 Tuesday, May 23, 3:00 PM - 5:00 PM

Down-Regulation of Neurodevelopment Related Genes in the Brain of Anorexia(anx/anx) Mutant Mice

Jun-Heon Park *College of Medicine, Kyung Hee University, Seoul, Korea, Department of Neuropsychiatry, Dept of psychiatry, KyungHee Univ.Hospital, #1 Hoegidong, Dongdaemoon-gu, Seoul, 130-702, Republic of Korea*, Sang-Min Lee, Geon-Ho Bahn, Ji-Young Song, Hwan-Il Chang, Kyung-Kyu Lee, Jong-Woo Kim

Educational Objectives:

At the conclusion of this presentation, participants know that down-regulation of neurodevelopment related genes in anorexia mice could be associated with phenotypes such as lethality, anorexia and growth failure observed in these mice

Summary:

Objective:

The aim of this study is to identify the candidate neurodevelopment related genes in anx/anx mice by cDNA microarray and confirm the expression of selected genes by RT-PCR and immunohistochemical method.

Method:

Microarray studies were performed on the whole brain of 21 days old homozygous anx/anx mice coming from heterozygous bleeder pairs(B6C3Fe-a/-a anx A/+a) obtained from the Jackson laboratory(Bar Harbor, ME, USA). Differentially expressed selected genes were then confirmed by using RT-PCR and immunochemistry

Result:

In cDNA microanalysis, anx/anx mice showed down-regulation of neurodevelopment related genes including Sox2(SRY-box containg gene 2) etc. RT-PCR analysis reproduced the results of cDNA microassay. Anx/anx mice showed significantly lower immunostaing intensities of Sox2. PDGF-α and E-cadherin in the PVN(paraventricular nucleus) of hypothalamus than those of control mice.

Conclusions:

These results suggest that the down regulation of neurodevelopment related genes in anorexia mice could be associated with phenotype such as lethality, anorexia and growth failure observed in these mice.

References:

1. Kim MJ, Kim Y, Kim SA, Lee HJ, Choe BK, Nam M, Kim BS, Kim JW, Yim SV, Kim CJ, Chung JH : Increases in cell proliferation and apoptosis in dentate gyrus of anorexia (anx/anx) mice.

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NR570 Tuesday, May 23, 3:00 PM - 5:00 PM

Weight Gain Associated With the α_{2a}- Adrenergic Receptor-1291 C/G Polymorphism and Olanzapine Treatment

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Educational Objectives:

To demonstrate a relationship between the -1291 C/G polymorphism of the α_{2a}adrenergic receptor and weight gain with olanzapine treatment.

Summary:

Weight gain can be an adverse effect of antipsychotics and is an important factor for long-term health and treatment compliance. Many reports have shown that the α_2-adrenergic receptor may be related to eating behaviors or lipolytic activities, both associated with body weight change. We hypothesized that there might be a relationship between the α_{2a}-adrenergic receptor -1291 C/G polymorphism and olanzapine induced weight gain. A group of 62 Korean schizophrenic patients participated in a study; weight and height measurements were obtained prior to starting olanzapine and measured again after long-term treatment. Genotyping for the -1291 C/G polymorphism was performed on all participants. Body weight changes from baseline to endpoint were significantly associated with genotypes ($p = 0.028$). The frequency of the G allele was significantly higher in subjects who had severe weight gain (defined as a more than 10% weight gain from baseline) compared to subjects who did not have extreme weight gain (less than 10% weight gain from baseline) ($X^2 = 6.120$, $P = 0.013$; OR= 2.58, 95% CI=1.21-5.51). Therefore, the findings from this study support a relationship between the -1291 C/G polymorphism of the α_{2a}-adrenergic receptor and weight gain in Korean schizophrenic patients receiving olanzapine treatment.

References:

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2. Reynolds GP, Zhang ZJ, Zhang XB. Polymorphism of the promoter region of the serotonin 5-HT(2C) receptor gene and clozapine-induced weight gain. Am J Psychiatry 2003; 160:677-679.

NR571 Tuesday, May 23, 3:00 PM - 5:00 PM

Double-Blind, Placebo- and Moxifloxacin-Controlled Crossover Study of the Effects of Desvenlafaxine Succinate on QT Interval in Healthy Adult Female Subjects

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to:

1. Understand the effects of desvenlafaxine succinate (DVS) on QT interval at therapeutic and supra-therapeutic doses
2. Understand the relationship between the pharmacokinetics of DVS and QT interval

Summary:

Objective: To assess the effect of desvenlafaxine succinate (DVS) at therapeutic and supra-therapeutic doses on QT interval.

Methods: In a randomized, double blind, single center, 4-period crossover study, healthy women aged 18 to 55 years were administered a single dose each of DVS 200 mg, DVS 600 mg, moxifloxacin 400 mg, and placebo, separated by a ≥5-day wash-out period. QT intervals were recorded by electrocardiogram; plasma samples were analyzed to evaluate pharmacokinetic parameters. PK/PD relationships, measured by association between drug concentration and QT intervals (n=68), were examined graphically. The primary endpoint was the 90% confidence intervals (CIs) for the difference between the active treatment and placebo on the change from baseline in QT 8 hours after administration. Baseline-adjusted QT intervals were analyzed using a mixed effects repeated measures analysis of covariance (ANCOVA) model.

Results: Seventy-one subjects were randomized and included in the safety population. DVS did not affect QT, as measured by Fridericia's correction (QTcF) and population-based correction (QTcN) at the primary efficacy endpoint (8 hours post-dose). Both DVS 200 and 600 mg groups produced 90% CIs that excluded and were less than 10 ms (ie, below the threshold at which QT effects are considered present). In contrast, moxifloxacin produced a statistically significant increase in QT versus placebo. The 90% CIs for both corrections were inclusive of and exceeded 10 ms, indicating that the study had assay sensitivity (ie, ability to demonstrate a positive QT effect for the active comparator). Graphic models yielded no evidence of a PK/PD relationship between drug concentration and QT interval for DVS and a positive relationship with moxifloxacin.

Conclusions: No effects on QT intervals were demonstrated in this study of healthy subjects treated with therapeutic and supra-therapeutic doses of DVS.

References:

1. Demolis JL, Kubitza D, Tenneze L, Funck-Bretano C: Effect of a single oral dose of moxifloxacin (400 mg and 800 mg) on ventricular repolarization in healthy subjects. Clin Pharmacol Ther 2000; 68:658-666.

2. Morganroth J: A definitive or thorough phase 1 QT ECG trial as a requirement for drug safety assessment. J Electocardiol 2004; 37:25-29.

NR572 Tuesday, May 23, 3:00 PM - 5:00 PM

A Randomized, Double-Blind, Placebo-Controlled Trial of Methylphenidate Extended Release (OROS MPH) in the Treatment of Antidepressant-Related Sexual Dysfunction

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Educational Objectives:

Educational objectives: At the conclusion of this presentation, the participants should be able to understand the potential role of augmentation with stimulants such as methylphenidate extended release (OROS MPH) for patients with major depression who have antidepressant-related sexual dysfunction.

Summary:

Objective: There are limited data to indicate effective treatment strategies for antidepressant-related sexual dysfunction. We studied whether augmentation with methylphenidate extended release (OROS MPH) improved sexual dysfunction associated with antidepressants in patients with treatment resistant major depression (TRD).

Methods: 60 TRD subjects were enrolled in a 4-week double-blind, placebo controlled trial of OROS MPH (18 mg -54 mg/day). The preexisting antidepressants were kept unchanged. The primary efficacy measure was the change in Arizona Sexual Experiences Survey (ASEX) from baseline to end of treatment in an ITT with LOCF approach.

Results: 83.3% of subjects completed the study. The mean dose of OROS MPH was 34.2 mg/day. The mean ASEX scores at baseline did not differ in the two groups (drug=22.4, placebo=23.5). There were no significant differences between the two groups in terms of changes in ASEX scores over time ($F(1, 35) = 1.14$, $p = 0.32$), although the numerical decrease in ASEX score was greater in OROS MPH (mean change=-4.5, 20.1% decrease) than in the placebo group (mean change=-0.6, 2.6% decrease). There was no correlation between improvement in HAM-D and ASEX scores. Combination of OROS MPH and antidepressants was well tolerated.

Conclusions: Augmentation with OROS MPH showed no statistically significant benefit in antidepressant-related sexual dysfunction. Addition of OROS MPH to antidepressants did not worsen preexisting sexual dysfunction. The negative findings should be interpreted in the context of a lack of power, short trial period and resistant nature of depression. Adequately powered, controlled trials are needed to fully evaluate the efficacy of OROS MPH in this area.

References

McGahuey CA, Gelenberg AJ, Laukes CA, Moreno FA, Delgado PL, McKnight KM, Manber R (2000). The Arizona Sexual Experience Scale (ASEX): reliability and validity. J Sex & Marital Therapy 26(1): 25-40.

References:

1. Modell et al. Comparative sexual side effects of bupriopion, fluoxetine, paroxetine, and sertraline. Clin Pharmacol 1997; 61:476-487.

2. McGahuey CA et al. The Arizona Sexual Experience Scale (ASEX): reliability and validity. J Sex & Marital Ther 2000; 26:25-40.

NR573 Tuesday, May 23, 3:00 PM - 5:00 PM

A Pooled Analysis of Outcome Predictors in the Short-Term Treatment of Panic Disorder With Venlafaxine XR or Placebo

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to:

1. Compare the efficacy and tolerability of venlafaxine XR compared with placebo in the treatment of panic disorder
2. Discuss the efficacy and tolerability of venlafaxine XR in the treatment of panic disorder
3. Evaluate potential predictors of panic disorder outcome measures

Summary:

Objective: To evaluate predictors of clinical outcomes in the short-term treatment of panic disorder.

Methods: In this pooled analysis of two 10-week flexible-dose studies and two 12-week fixed-dose studies, 1595 adult outpatients with DSM-IV panic disorder (± agoraphobia) were randomly assigned to treatment with venlafaxine (Effexor®) XR 75, 150, or 225 mg/day or placebo. Predictors included panic severity (full-symptom panic attack frequency <8 or ≥8 panic attacks during each 2 week period in the 4 weeks prior to baseline) and gender. Other predictors included Panic Disorder Severity Scale (PDSS) score; and scores for CGI-I and CGI-S; HAM-A total, somatic, and psychic anxiety; HAM-D_{17} total and depressed mood item; and Phobia Scale fear, avoidance, and overall phobia state. The primary efficacy measure was the proportion of patients free of full-symptom panic attacks.

Results: Significantly ($P<0.05$) higher proportions of low severity patients than high severity patients and men than women were panic-free at endpoint in the venlafaxine XR and placebo groups. For nearly all baseline and endpoint clinical ratings, greater mean severity was associated with lower proportions of panic-free patients, in both groups.

Conclusions: Gender and baseline panic disorder severity, and most baseline and endpoint clinical ratings predicted panic-free status at endpoint.

References:

1. Bradwejn J, Ahokas A, Stein DJ, Salinas E, Emilien G, Whitaker T: Venlafaxine extended-release capsules in panic disorder: flexible-dose, double-blind, placebo-controlled study. Br J Psychiatry 2005; 187:352-359.
2. Pollack MH, Rapaport MH, Fayyad R, Otto MW, Nierenberg AA, Clary CM: Early improvement predicts endpoint remission status in sertraline and placebo treatments of panic disorder. J Psychiatr Res 2002; 36:229-236.

NR574 Tuesday, May 23, 3:00 PM - 5:00 PM

Is Multiple-Daily Dose Enteric-Coated Divalproex Truly More Protective Than Extended-Release Dosed Once-Daily When a Dose Is Missed in the Manic Patient? Evidence From Comprehensive Plasma Valproic Acid Concentration Simulations

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Educational Objectives:

1) Compare and contrast differences predicted for total plasma valproic acid (VPA) concentrations from two distinct formulations of divalproex sodium (enteric-coated tablets [Depakote®, Abbott Labs] administered twice-daily and once-daily extended-release tablets [DepakoteER®, Abbott Laboratories), when a dose(s) is (are) missed and subsequently replaced.

2) Discuss the clinical significance of such changes in total plasma VPA concentrations in the patient with bipolar mania treated with either formulation of divalproex sodium.

3) Learn potential value of computer simulation of changes in VPA concentration using published population parameter values when objective, real-time study of such a clinical situation is not ethical or possible.

Summary:

Rationale. Higher steady-state total plasma valproate concentrations [VPA] are associated with greater efficacy in mania. Missing and replacing [m/r] at a later time, enteric-coated divalproex (Divalproex®, Abbott, [dvp]) dose(s)compared to m/r extended-release divalproex (Divalproex-ER®, [dvp-ER]) may have different ability to sustain [VPA]. Computer-simulated changes in [VPA] upon m/r dose(s) of twice-daily dvp were compared to m/r once-daily dvp-ER to determine which formulation better sustains [VPA].

Methods. We included virtual adult mania patients (N=1000), taking dvp 562.5mg q12h, versus dvp-ER 1250mg qam (higher dvp-ER dose compensates for lower bioavailability) chronically as monotherapy (uninduced); likewise, polytherapy (hepatic enzyme-induced) patients, taking 1125mg dvp q12h versus 2500mg dvp-ER qam. [VPA] was analyzed when dose(s) were m/r at 12, 18, 24h, while resuming scheduled therapy at 24h, via a published, comprehensive simulation methodology.

Results. In induced patients, steady-state baseline (no m/r dose) mean [VPA] Cmin and Cmax values for dvp were 67 and 98 mg/L; for dvp-ER, 81 and 88 mg/L, respectively. When dvp dose(s) were missed, mean [VPA] fell to 37, 28, 20 mg/L at 12, 18, 24h, respectively. Replacing/resuming dvp increased the mean [VPA] to 113, 117, 129 mg/L (same times); mean maximum increase =31 mg/L above baseline Cmax. When a dvp-ER dose was missed, mean [VPA] fell to 46, 34, 25 mg/L (same times). Replacing/resuming dvp-ER bumped mean [VPA] to 107, 111, 114 mg/L(corresponding times); maximum mean increase =26 mg/L above baseline Cmax. When dvp doses or a dvp-ER dose is m/r at 24 h, 90% of patients would have a [VPA] Cmax increment of <43 or <33 mg/L, for dvp or dvp-ER, respectively. In uninduced patients, [VPA] changes were similar, but less pronounced.

Conclusions. Our simulations predict multiple-daily dvp is not more protective than daily dvp-ER for equal durations and equivalent doses of missed therapy with respect to maintenance of [VPA].

References:

1. Allen M, et.al. Linear Relationship of Valproate Serum Level to Response and Optimal Levels in Acute Mania. Am J Psych 2006, in press.
2. Reed RC and Dutta S. Predicted Serum Valproic Acid Concentrations in Patients Missing and Replacing a Dose of Extended-Release Divalproex Sodium. Am J Health-Syst Pharm 2004; 61:2284-9.

NR575 Tuesday, May 23, 3:00 PM - 5:00 PM

Difference in Weight Change and Hypersalivation Between FazaClo® (clozapine, USP) Orally Disintegrating Tablets and Solid Oral Clozapine Tablets

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Educational Objectives:

Presentation of these findings should alert the profession to the fact that the orally disintegrating form of clozapine may avoid the weight gain that is characteristic of solid oral forms of clozapine and other antipsychotics and thus limit the risk of metabolic syndrome.

Summary:

Introduction: This retrospective study was undertaken to identify possible variations in weight change and hypersalivation between FazaClo Orally Disintegrating Tablets and solid oral clozapine tablets. Methods: The charts of patients diagnosed with schizophrenia or schizoaffective disorder and living in a long-term care facility were reviewed. Patients on a prior medication regimen of clozapine tablets had begun FazaClo at the same daily dose. They were weighed on the same calibrated scale while on solid oral clozapine tablets and then 4-weeks after starting FazaClo Orally Disintegrating Tablets. Results of a scale used to assess changes in salivation and nighttime drooling were also reviewed for all patients. Results: 20 patientsÃ¢â'¬â,¢ charts (comprised of 14 males and 6 females) were reviewed. Mean age was 54 and all were diagnosed with schizoaffective disorder. Four-weeks after starting FazaClo, 18 patients (90%) showed weight reduction (mean weight loss 7.6 lbs +/- 3.9 lbs) while 2 patients experienced no change in weight. Seven of the 20 patients (38.9%) had mild-to-severe hypersalivation on the solid oral clozapine tablets and all of these patients experienced a reduction in the intensity of hypersalivation 4-weeks after starting FazaClo. Of these, 6 suffered from nighttime drooling which was absent 4-weeks after starting FazaClo. Conclusions: FazaClo Orally Disintegrating Tablets appear to be associated with both weight reduction and a decreased intensity of hypersalivation and nighttime drooling compared to that with solid oral clozapine tablets. Further longitudinal data are in the collection phase.

References:

1. Journal Article: Haddad, P: Weight Gain with Atypical Antipsychotics in the Treatment of Schizophrenia. Journal of Psychopharmacology 2005; 19:16-27.
2. Journal Article: Freudenreich, O: Drug-induce Sialorrhea. Drugs Today 2005; 41: 411-418.

NR576 Tuesday, May 23, 3:00 PM - 5:00 PM

Evaluation of Long-Acting Injectable Risperidone for Older Adult Inpatients With Psychosis

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Educational Objectives:

This is a retrospective pilot study evaluating the effectiveness of risperidone long-acting injection in an older inpatient population with chronic psychosis.

At the conclusion of this presentation, the participant should be able to recognize the possible utility and benefit of long-acting injectable risperidone in treating a chronically psychotic and older inpatient population.

Summary:

Introduction:

The treatment of the older adult patient with chronic psychosis with the long-acting formulation of risperidone in the inpatient setting has not been fully evaluated to date. The authors report a retrospective pilot study evaluating the effectiveness of risperidone long-acting injection in such a psychiatric treatment setting.

Objective:

To assess the effectiveness of long-acting injectable risperidone in an older adult inpatient population with psychosis.

Methods:

This is a retrospective assessment of patients aged 50 years and older admitted to an inpatient psychiatric facility for severe and unstable psychosis. Clinical judgment prompted the initiation of the long-acting injectable form of risperidone. Per hospital policy, baseline and follow-up assessments utilizing the Positive and Negative Syndrome Scale (PANSS) was done. Physician clinical assessment of response is reflected using the Clinical Global Impression Scales for Severity and Improvement (CGI-S/I).

Results:

These are the preliminary findings of twenty-five older adults who were treated with risperidone long-acting injection for at least 2 months in an inpatient setting.

Schizophrenia was the diagnosis for 76% (n=19) of the patients. Other patients were diagnosed with either bipolar disorder with psychotic features or with schizo-affective disorder. The mean age was 59.5 years (range: 50 - 76 yrs). The mean of the total PANSS scores at baseline was 105 (SD +/- 28.3, n=20). The mean total PANSS scores at last follow-up was 86.3 (SD +/- 27, n=20). The difference in total PANSS scores was statistically significant ($p<0.01$). For the patients receiving a CGI-Improvement assessment (n=15), 67% were either much improved or very much improved at last follow-up. The mean dose of risperidone long-acting injection was 36.5 mg. Further descriptions and sub-analyses of this evaluation will be presented.

Conclusions:

Long-acting risperidone was associated with clinically and statistically significant improvements in a group of older adult inpatients with psychosis.

References:

1. Kane JM et al. Long-acting injectable risperidone: efficacy and safety of the first long-acting atypical antipsychotic. Am J Psychiatry. 2003;160:1125-1132.
2. Fleischhacker WW et al. Treatment of schizophrenia with long-acting injectable risperidone: a 12-month open-label trial of the first long-acting second generation antipsychotic. J Clin Psychiatry. 2003;64:1250-1257.

NR577 Tuesday, May 23, 3:00 PM - 5:00 PM

The Relationship Between Serotonin and Glutamate System Genes and Drug Response in OCD

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Educational Objectives:

1. At the conclusion of this presentation, the participant should be able to appreciate the current status of genetic research in Obsessive Compulsive Disorder (OCD).

2. At the conclusion of this presentation, the participant should be able to appreciate how utilizing drug response information may assist in genetic research in OCD.

Summary:

Introduction: Efforts to identify susceptibility genes in OCD have met with limited success to date. In part, this work has been hampered by the need to generate potential candidates based on etiological models of the illness, and the challenge imposed by likely phenotypic and genetic heterogeneity. A promising alternative strategy is to investigate the relationship between inter-individual genetic variation and drug response. *Methods:* In this study,

retrospective response data on multiple 5HT reuptake inhibitors was collected in 107 individuals meeting DSM-IV criteria for OCD. All individuals were genotyped for multiple polymorphisms in the 5HT transporter gene (5HTTLPR), 5HT 1Dβ (5HT1Dβ) receptor, and glutamate system genes GRIN2B and the transporter SLC1A1. Individuals were grouped into those who were "much" or "very much" improved following an adequate trial of one or more medications as compared with those who reported "minimal", "no change" or "worsening" in response to all medications tried. This was followed by exploratory analyses on a drug-by-drug basis. *Results:* In total, N=70 individuals had complete data for trials of one or more medication. Results were suggestive of a relationship between drug response and 5HTTLPR (Fisher's exact test p= 0.153). When analyzing responses to individual drugs, results were significant for clomipramine (N= 35) and 5HT1Dβ (-161A/T) (χ^2 = 6.198, df= 2, p= 0.045). A significant result was also obtained for individuals who had trial data for citalopram (N= 14) and GRIN2B ((HaeIII) (χ^2 =6.873, df= 2, p= 0.032). *Conclusion:* These data support the utility of the pharmacogenetics approach, and previous work suggesting a role for 5HTTLPR, 5HT1Dβ, and GRIN2B in vulnerability to OCD.

References:

1. Mundo, E., Richter, M.A., Zai, G., et al. The 5HTIDb Receptor Gene is Implicated in the Pathogenesis of Obsessive-Compulsive Disorder: Further Evidence from a Family-Based Association Study. Mol Psychiatr, 7:805-809, 2002.
2. Arnold, P.D., Zai, G., Richter, M.A. Genetics of Anxiety Disorders. Current Psychiatry Reports, 6(4):243-254, 2004.

NR578 Tuesday, May 23, 3:00 PM - 5:00 PM

Determinants in Antidepressant Treatment Selection Following the Introduction of Duloxetine

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize variations between duloxetine initiators and other select medications in terms of demographics, prior medical comorbidities, and treatment history in the first four months after duloxetine was introduced to the US marketplace. Also, participants will learn factors associated with duloxetine initiation versus individual drug cohorts (venlafaxine XR, buproprion, SSRIs, and escitalopram).

Summary:

Objective. To compare factors associated with antidepressant treatment selection for patients initiating on duloxetine versus venlafaxine XR, bupropion, and SSRIs.

Methods. Retrospective claims were assessed for adults, with and without depression diagnoses, initiating on new prescriptions for select antidepressants between 8/31/04 to 12/31/04. Diagnostic and treatment histories were established through prior claims (12 months before index medication date).

Results: Of the 230,738 eligible patients, 29.7% had depression, 71.4% were female, mean age was 44.6 years, and 77.9% initiated on SSRIs. Using logistic regression models for the depression cohort, patients initiating on duloxetine (n=2061) versus all other initiators were older, had more pain, depression-related, MDD recurrent episode diagnoses; more pain medications, antidepressants, and any psychotherapy (all p<.01). Duloxetine patients also initiated therapy later in the study and were more often prescribed therapy by mental health or other specialists versus primary care. When depressive diagnoses were absent, duloxetine patients (n=2346) versus other antidepressant initiators (n=162,212) were more likely to be female. All other determinants of antidepressant use remained consistent. *Conclusions.* In the first four months after launch, duloxetine initiators were associated with worse prior diagnostic and treatment histories. Case mix adjustments should be made when comparing drug cohorts.

References:

1. 1. Detke MJ, Lu Y, Goldstein DJ, McNamara RK, Demitrack MA: Duloxetine 60mg once daily dosing versus placebo in the acute treatment of major depression. Journal of Psychiatric Research 2002; 36: 383'390.
2. 2. Bair M, Robinson RL, Kroenke K, Katon W: Depression and pain comorbidity: A literature review. Arch Gen Med 2003; 163:2433-2445.

NR579 Tuesday, May 23, 3:00 PM - 5:00 PM

Sleep Laboratory Assessment of Indiplon in Primary Insomnia: Results of a Double-Blind, Placebo-Controlled, Crossover Trial

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Educational Objectives:

The research data presented will contribute to the participant's understanding of the safety and efficacy of treatment of DSM-IV primary insomnia with indiplon.

Summary:

Introduction: To evaluate the efficacy of indiplon, a novel Gamma-aminobutyric acid $_A$ receptor modulator, in patients diagnosed with primary insomnia characterized by sleep maintenance difficulties.

Methods: Patients (N=100; mean age, 51 years, range, 22-78 years; female, 63%) who met DSM-IV criteria for primary insomnia, and who reported >60 minutes of wake time after sleep onset, were randomized to a double-blind, 2-period, 2-night crossover sleep lab comparison of indiplon 15mg and placebo. Polysomnographic assessments included wake time during sleep (WTDS, primary outcome), wake time after sleep onset (WASO), latency to persistent sleep (LPS), total sleep time (TST), and sleep quality. Comparisons were made using a crossover ANOVA model.

Results: Treatment with indiplon was associated with significantly reduced WTDS (60.4 + 3.5 min versus 71.5 + 3.6 min; p= 0.0036), reduced WASO (73.9 + 4.0 min versus 83.0 + 4.0 min; p=0.019), significantly shorter LPS (12.5 + 1.1 min versus 26.1 + 2.4 min; p<0.0001), and significantly longer TST (389.8 + 4.9 min versus 362.8 + 5.0 min; p<0.0001) relative to placebo. Sleep quality was rated as significantly improved on indiplon (3.3 + 0.1) compared to placebo (4.0 + 0.1; p<0.0001). The overall incidence of adverse events was similar on indiplon (8.0%) and placebo (10.4%).

Conclusions: The 15 mg dose of indiplon was safe and effective in inducing and maintaining sleep in patients with primary insomnia.

References:

1. Foster AC, Pelleymounter MA, Cullen MJ, Lewis D, Joppa M, Chen TK, Bozigian HP, Gross RS, Gogas KR. In vivo pharmacological characterization of indiplon, a novel pyrazolopyrimidine sedative-hypnotic. J Pharmacol Exp Ther 2004;311:547-559.
2. Simon GE, VonKorff M. Prevalence, burden, and treatment of insomnia in primary care. Am J Psychiatry 1997;154:1417-1423.

NR580 Tuesday, May 23, 3:00 PM - 5:00 PM

Efficacy and Safety of Doxepin 1, 3, and 6 mg in Elderly Adults With Primary Insomnia

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to evaluate the safety and efficacy of sub-therapeutic doses of doxepin on measures of sleep for the treatment of insomnia in elderly adults.

Summary:

Introduction: This randomized, placebo-controlled cross-over study evaluated the efficacy and safety of doxepin in elderly adults with insomnia.

Methods: Randomized patients (n=76) reported ≥3 months of DSM-IV primary insomnia; they additionally had ≥60 minutes of wake-time-during-sleep (WTDS), 240-410 minutes of total-sleep-time (TST), and ≥10 minutes of latency-to-persistent-sleep (LPS), confirmed by polysomnography (PSG). Patients received a random sequence of doxepin 1mg, 3mg, 6mg or placebo. Treatment periods consisted of two PSG assessment nights with a 5- or 12-day drug-free interval. Primary endpoint was WTDS; secondary endpoints included wake-after-sleep-onset (WASO), TST, and LPS.

Results: All three doxepin groups had significantly improved WTDS ($p \leq 0.0001$), WASO ($p < 0.0001$), and TST ($p < 0.0001$) versus placebo. LPS was numerically reduced; subjective sleep latency was significantly reduced ($p = 0.02$) in the doxepin 6mg group. The pattern of the remaining subjective efficacy results was consistent with PSG. There were no significant group differences in next-day residual sedation, adverse events were not different among groups, and sleep architecture was generally preserved.

Conclusions: In elderly adults with insomnia, doxepin 1, 3, and 6mg was well-tolerated and produced significant improvement in PSG-defined and patient-reported sleep maintenance and duration endpoints that persisted through the final third of the night (including hour 8) without hangover/next-day residual effects.

References:

1. Ancoli-Israel S, Roth T: Characteristics of insomnia in the United States: results from the 1991 National Sleep Foundation Survey I. Sleep 1999; 22 Suppl 2:S347-S353.
2. Carskadon MA, et al: Sleep fragmentation in the elderly: Relationship to daytime sleep tendency. Neurobiol Aging 1982;3:321-7.

NR581 Tuesday, May 23, 3:00 PM - 5:00 PM

Armodafinil Does Not Affect Intended Sleep as Determined by Polysomnography in Patients With Excessive Sleepiness

Thomas Roth, Ph.D. *Henry Ford Hospital, 2799 West Grand Boulevard, CFP3, Detroit, MI, 48202*, Timothy A. Roehrs, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that armodafinil does not influence sleep when sleep is desired in patients with excessive sleepiness associated with narcolepsy, obstructive sleep apnea/hypopnea syndrome, or shift work sleep disorder.

Summary:

Introduction/Hypothesis: Armodafinil (the *R*-enantiomer of racemic modafinil) is a wake-promoting agent. Armodafinil (200 mg) has higher plasma concentrations later in the day relative to modafinil (200 mg). The effects of armodafinil on intended sleep determined by polysomnography are reported.

Methods: Four 12-week, double-blind, placebo-controlled, multicenter studies evaluated armodafinil (150 and 250 mg/day; n=1090). Nocturnal (narcolepsy, obstructive sleep apnea/hypopnea syndrome [OSA/HS]) or daytime (shift work sleep disorder [SWSD]) polysomnographic data were collected at baseline and week 12. Armodafinil was administered at 0700 hours daily (narcolepsy and OSA/HS) or within 30 minutes of 2200 hours on the night shifts worked (SWSD).

Results: Mean change from baseline in the latency to persistent sleep was -0.6, -1.6, and 3.1 minutes for the armodafinil group and 7.2, -0.3, and 1.1 minutes for the placebo group in the narcolepsy, OSA/HS and SWSD studies, respectively. Mean number of arousals were decreased in all 3 patient populations (change from baseline, armodafinil -0.5 to -1.7 versus placebo -0.1 to -1.5). The mean change in sleep efficiency was -0.6%, -0.4%, and -2.1% for armodafinil versus -0.9%, -0.7%, and 0.5% for placebo in the narcolepsy, OSA/HS, and SWSD groups, respectively. Mean changes in wake after sleep onset were not clinically meaningful with armodafinil compared with placebo (narcolepsy, 3.5 versus -3.6 min; OSA/HS, 1.7 versus 1.7 min; SWSD, 6.2 versus -4.7 min). Sleep architecture was unaffected by armodafinil.

Conclusions: Armodafinil does not adversely affect sleep when sleep is desired in patients with excessive sleepiness.

Funding Source: Sponsored by Cephalon, Inc.

References:

1. Rechtschaffen A, Kales A: A Manual of Standardized Terminology, Techniques and Scoring System for Sleep Stages of Human Subjects. Los Angeles, CA: UCLA Brain Information Service/Brain Research Institute; 1968.
2. Mitler MM, Gujavarty KS, Browman CP: Maintenance of Wakefulness Test: a polysomnographic technique for evaluation treatment efficacy in patients with excessive somnolence. Electroencephalogr Clin Neurophysiol 1982; 53:658-61.

NR582 Tuesday, May 23, 3:00 PM - 5:00 PM

The Effect of Eszopiclone 3 mg Compared With Placebo in Patients With Rheumatoid Arthritis and Co-Existing Insomnia

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to evaluate the effects of 4 weeks of treatment with eszopiclone 3mg on sleep efficacy measures, daytime function, pain, and rheumatoid arthritis disease activity in patients with rheumatoid arthritis.

Summary:

Objective: Patients with rheumatoid arthritis (RA) often report co-existing insomnia. This pilot study was conducted to evaluate the efficacy and safety of eszopiclone 3mg in patients with RA and co-existing insomnia.

Methods: This multicenter, double-blind, study enrolled patients aged 25-64 years with ACR-defined RA (receiving treatment for ≥3 months) who reported insomnia (wake time after sleep onset (WASO) ≥45 min & total sleep time (TST) ≤6.5 hr). After placebo run-in, patients were randomized to eszopiclone (n= 77) or placebo (n=76) nightly for 4 weeks, followed by a 2-week run-out. Patient reports of sleep (sleep latency [SL], WASO, TST),

Insomnia Severity Index (ISI), daytime function, pain, and RA assessments were evaluated.

Results: Eszopiclone (vs placebo) significantly reduced SL ($p<0.0001$), WASO ($p=0.0002$), and nocturnal awakenings ($p=0.0065$), and significantly increased TST ($p=0.0001$), sleep depth ($p=0.0003$), sleep quality ($p<0.0001$), daytime alertness, ability to function, and ability to concentrate (all $p<0.04$). ISI total scores were significantly better ($p<0.0001$) with eszopiclone versus placebo, as were individual items of sleep quality, feeling rested, daytime fatigue, relationship enjoyment, and sleep difficulties (all $p<0.02$). Change scores on the Arthritis Self Efficacy Scale were clinically and statistically significant for overall score ($p=0.046$), pain ($p=0.0064$), and pain and other symptoms ($p=0.018$). No differences in duration or severity of morning stiffness were noted, though subjects' assessment of pain severity was significantly reduced with eszopiclone ($p=0.023$). Number of tender joints was also significantly reduced in the eszopiclone group ($p=0.035$). Subject global assessments were also better with eszopiclone, though not statistically significant ($p=0.072$).

Conclusion: In this pilot study of RA and co-existing insomnia, eszopiclone 3mg improved all sleep efficacy measures and daytime function over the treatment period. In addition, patients treated with eszopiclone experienced reductions in some measures of pain and RA disease activity.

Support for this study provided by Sepracor Inc.

References:

1. Krystal AD, Walsh JK, Laska E, Caron J, Amato DA, Wessel TC, Roth T: Sustained efficacy of eszopiclone over 6 months of nightly treatment: results of a randomized, double-blind, placebo-controlled study in adults with chronic insomnia. Sleep 2003;.
2. Zammit GK, McNabb LJ, Caron J, Amato DA, Roth T: Efficacy and safety of eszopiclone across 6-weeks of treatment for primary insomnia. Current Medical Research and Opinion 2004; 20(12):1979-1991.

NR583 Tuesday, May 23, 3:00 PM - 5:00 PM

Reboxetine Augmentation in Resistant Depression to SSRIs, Venlafaxine, and Mirtazapine

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Educational Objectives:

At the conclusion of this presentation, the participant will have greater information on the possibility of treating resistant-depression with combination therapy.

Summary:

Objective: To evaluate efficacy of the combination therapy with two antidepressants from different pharmacological families in treatment-resistant depressive patients.

Methods: In this prospective 12 weeks open-label study, we assessed the effectiveness of the addition of reboxetine to 195 depressive patients that had previously not responded, or had done so only in a partial way, to conventional treatment, in monotherapy, with SSRIs (fluoxetine n=29; paroxetine n=44; sertraline n=30; citalopram n=38), venlafaxine (n= 40) or mirtazapine (n= 14). Data were analyzed on an intent-to-treat basis, using the last-observation-carried-forward (LOCF) method.

Results: Mean decrease on the 21-items Hamilton Depression Rating Scale (HDRS) score was 58.02%, and on the Clinical Global Impressions Scale (CGI), 63.41%. At the end of the treatment, 78.7% of the patients were evaluated as improvement (CGI < 4), 42.6% as responders (HDRS $\leq 50\%$) and 33% in remission (HDRS ≤ 10). No serious side effects were observed during combination therapy, being more frequent increased constipation (8.5%) and dry mouth (5.3%).

Conclusions: The results of this study show that the strategy of combination with reboxetine may be an effective and well-tolerated tool in treatment-resistant patients who have failed to adequately respond to monotherapy with SSRIs, venlafaxine or mirtazapine.

References:

1. Rubio G, San L, López-Muñoz F, Alamo C. Reboxetine adjunct for partial or nonresponders to antidepressant treatment. Journal of Affective Disorders 2004; 81: 67-72.
2. Lucca A, Serreti A, Smeraldi E: Effect of Reboxetine augmentation in SSRI resistant patients. Human Psychopharmacol Clin Exp 2000; 15:143-145.

NR584 Tuesday, May 23, 3:00 PM - 5:00 PM

Metrics for Clinical Effectiveness in Bipolar Disorder

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Educational Objectives:

At the conclusion of this presentation, the participant will be familiar with measures of the clinical effectiveness of psychotropic medications commonly used for Bipolar Disorder (BP).

Summary:

Objective: Outcomes of bipolar disorder tend to focus on either depressive or manic symptoms, but not both. The purpose of this study is to explore more clinically relevant metrics of effectiveness of medications prescribed for bipolar disorder in a specialty clinic.

Methods: Percentage achieving a clinical status of recovering (euthymia) within 3 months and percentage meeting DSM IV criteria for recovered within 12 months who were treated with a variety of medications were compared for subjects having ≥4 visits. Duration of each new trial of classes of medications was determined from start to date of last use. Data were analyzed with ANOVA and chi-square tests as appropriate.

Results: BP subjects (N= 425; 67% BP I) were treated and followed as per their clinician. Overall, 78% met criteria for recovering within 3 months, and 73% recovered over 12 months. The median duration of use in days, percent recovering within 3 months, and percent recovered within 12 months for each class of medications respectively were: Lithium (n=48), 167, 60%, 50%; Valproate (n=39) 164, 67% 54%; Lamotrigine (n=88) 207, 81%, 61%; Atypical antipsychotics (n=290), 99.5, 62%, 46.5%; Antidepressants (n=220) 112, 68%, 51%; and anxiolytics (n=93) 127, 65%, 47%. Duration of use and percentage recovering at 3 months treated with lamotrigine were significantly greater than atypical antipsychotics, or antidepressants ($p < .01$, $p < .05$).

Conclusions: Using duration of use and percent recovering on treatment as metrics of clinical effectiveness, lamotrigine appeared to result in better long term outcomes than those prescribed either antipsychotics or antidepressants.

References:

1. Sachs GS, Strategies for improving treatment of bipolar disorder: integration of measurement and management Acta Psychiatr Scand Suppl. 2004 Sep;(422):7-17.

2. Sachs GS, Guille C, McMurrich SL. A clinical monitoring form for mood disorders. Bipolar Disord. 2002;4:323-327.

NR585 Tuesday, May 23, 3:00 PM - 5:00 PM

Use of Alcohol in VA Medical Centers for Alcohol Withdrawal

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Educational Objectives:

Objectives:

To report the data that suggests that alcohol should not be used for the prevention and or treatment of alcohol withdrawals.

To report the prevalence of availability of alcohol at academic medical centers' pharmacy formularies.

To report the prevalence of the availability of alcohol on VA formularies.

To report the absence of a central policy on the use of alcohol for the prevention/treatment of alcohol withdrawals in the VA system.

Summary:

Objectives:

To report the data that suggests that alcohol is widely available for use for the prevention and or treatment of alcohol withdrawals within the VA Medical system.

To report the prevalence of availability of alcohol at academic medical centers' pharmacy formularies.

To report the prevalence of the availability of alcohol on VA formularies.

To report the absence of a central policy on the use of alcohol for the prevention/treatment of alcohol withdrawals in the VA system.

The purpose of this study is to ascertain how widely alcohol is available on the VA medical centers, either through their formulary or a non-formulary process. Also, to investigate how the alcohol is obtained, and administered to the patients. Also to determine who are the most common prescribers of alcohol for the detoxification/treatment of alcohol dependence.

Method:

The pharmacy directors at each of the VA medical center across the United States was contacted by mail/email/phone/fax, and asked to complete a specially developed questionnaire. Responses were entered in a database, and frequencies determined. Data was also analyzed for geographic relationship and availability of alcohol.

Results:There is no central VA wide policy on the use of alcohol for prevention/treatment of alcohol withdrawals. Only 9% of the VA medical Centers had a policy against the use of alcohol. Alcohol was available in almost 50% of the VA Medical centers through formulary or non-formulary process. Pharmacy was most often responsible for its procurement. Nursing was most often responsible for its administration. Internists were the most common prescribes, followed by surgeons.

References:

1. Blondell RD, Dodds HN, Blondell MN, Looney SW, Smoger SH, Sexton LK, Wieland LS, Swift RM. Ethanol in formularies of US teaching hospitals.JAMA. 2003 Feb 5;289(5):552.

2. Smoger SH, Looney SW, Blondell RD, Wieland LS, Sexton L, Rhodes SB, Swift RM. Hospital Use of Ethanol Survey (HUES): preliminary results. J Addict Dis. 2002;21(2):65-73.

NR586 Tuesday, May 23, 3:00 PM - 5:00 PM

Relationship Between Agitation Severity and Ziprasidone(Geodon) Treatment Response in Patients With Schizophrenia

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Educational Objectives:

At the conclusion of this presentation, the participants will have a greater understanding of the relationship between agitation severity and treatment response in schizophrenia

Summary:

Objective: Agitation is a common antipsychotic treatment target. We evaluated the relationship between agitation severity and ziprasidone treatment response in patients with schizophrenia.

Methods: Pooled analyses of 2 randomized, double-blind, fixed-dose, placebo-controlled, 6-week trials of ziprasidone (40 mg to 160 mg/day) were performed. Using statistical interaction analysis, treatment response was evaluated in patients with moderate to high (PANSS excitement EC score > 15, N=182) and low (PANSS EC score < 15, N=358) agitation severity at baseline. Overall improvement was assessed using the CGI-S scale. The contribution of improvement in agitation to the change in CGI-S due to ziprasidone treatment was evaluated using mediator analyses.

Results: Ziprasidone treatment resulted in significant improvement in CGI-S (LOCF) compared with placebo, in patients with both high and low baseline agitation scores. After correcting for placebo responses, effect size for CGI-S change was -0.63 and -0.24 in high and low agitation subgroups, respectively ($p=0.039$). Improvement in CGI-S was found to be mediated by change in agitation ($p<0.001$), which accounted for 37% of the total treatment effect on CGI-S.

Conclusions: These findings suggest that overall response to ziprasidone is in part mediated by effects on agitation symptoms. Further studies are needed to explore if this effect is ziprasidone-specific or is applicable to other antipsychotics.

References:

1. Lindenmayer JP, Brown E, Baker RW et al: An excitement subscale of the positive and negative syndrome scale. Schizophrenia Research 2004; 69:331-337.:.

2. Kraemer HC, Wilson T, Fairburn OG et al: Mediators and moderators of treatment effects in randomized clinical trials. Arch Gen Psychiatry 2002;59:877-883.

NR587 Tuesday, May 23, 3:00 PM - 5:00 PM

Asenapine: A Novel Psychopharmacologic Agent With a Unique Human Receptor Signature

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to:

1. Describe the receptor signature of asenapine.
2. Compare the receptor signature of asenapine with those of currently available antipsychotic drugs.

Summary:

Objective: Preliminary trials suggest that asenapine offers an advance in treating schizophrenia. We explored the mechanism

of action of asenapine by comparing its human receptor signature with the receptor-binding profiles of antipsychotic drugs.

Methods: We determined the binding affinities of asenapine under comparable assay conditions for cloned human serotonergic, alpha-adrenergic, dopaminergic, histaminic, and muscarinic receptors. In all, asenapine has been tested in more than 90 receptor assays (including enzyme, transporter, and ion channel) for determining receptor specificity.

Results: The rank order of receptor affinity for asenapine at the various receptors was different from that of olanzapine, risperidone, quetiapine, aripiprazole, ziprasidone, clozapine, and haloperidol. Asenapine exhibited a higher affinity (Ki in nM) for 5-HT_{2C} (0.03), 5-HT_{2A} (0.07), 5-HT_7 (0.11), 5-HT_{2B} (0.18), 5-HT_6 (0.25), and 5-HT_7 (0.11) receptors with reference to D_2 (1.3) receptors. Receptor affinities for the antipsychotic drugs tested were generally in agreement with published data. Compared with antipsychotic drugs, asenapine is likely to have more potent interaction with 5-HT_{2C}, 5-HT_7, 5-HT_6, 5-HT_5 (1.6) and D_3 (0.42) receptors and α_1 (1.20) and α_2 (0.33-1.2) adrenoceptors. Unlike olanzapine, clozapine, and quetiapine, asenapine has much lower affinity for muscarinic receptors relative to its D_2 affinity, suggesting a low propensity for anticholinergic adverse effects. Asenapine was inactive in all other receptor assays tested for determining general receptor specificity.

Conclusions: The human receptor signature of asenapine differs from that of the antipsychotics tested, with potent interactions at an ensemble of serotonergic, dopaminergic, and alpha-adrenergic receptors, but no significant interaction at muscarinic receptors. These characteristics may contribute to the clinical effectiveness and tolerability of asenapine in patients with schizophrenia and bipolar disorder.

Funding Source: This study was supported by Organon Laboratories Ltd and Pfizer Inc.

References:

1. Kongsamut S, Kang J, Chen XL, Roehr J, Rampe D: A comparison of the receptor binding and HERG channel affinities for a series of antipsychotic drugs.Eur J Pharmacol 2002; 450:37-41.
2. Potkin SG, et al: Asenapine, a novel psychopharmacologic agent with efficacy in positive and negative symptoms during acute episodes of schizophrenia: a randomized placebo- and risperidone-controlled trial. Annual Meeting of the ACNP, 12/11-15/05.

NR588 Tuesday, May 23, 3:00 PM - 5:00 PM

A Ten-Year Study of the Pattern of Use and Adherence to Antipsychotic Drugs in a Korean General Hospital

Sang-Eun Shin, M.D. *Incheon Christian Hospital, Department of Psychiatry, 237, Yul Mok-Dong, Choong-Ku, Incheon, 400-714, Republic of Korea*, Kun Jung, M.D., Kye-Sung Lee, M.D.

Educational Objectives:

This study was investigated the change in the antipsychotic drug use pattern and its effect on adherence during ten years. The study was a retrograde analysis and had limitation. But this demonstrated the relationship between antipsychotic drugs and adherence and drug use pattern in Korea

Summary:

Introduction: This study examined the change in the antipsychotic drug use pattern and its effect on adherence.

Methods: The subjects were 523 schizophrenic patients who had been hospitalized at some time between 1994 and 2003. The study was a retrograde analysis of the antipsychotic dose, combination rate, and dose of adjuvant drugs. To examine adherence, we investigated the duration of hospitalization, follow-up rate, duration of follow-up, and relation to antipsychotic drugs.

Results: The use of antipsychotic drugs increased with time. The combination rate was not significant. The dose of olanzapine increased with time (r=.86, $p<.05$). Of the adjuvant drugs, the dose of propranolol increased with time (r=.74, $p<.05$). Clozapine use involved more hospitalization days than risperidol or standard antipsychotic drugs (Quetiapine and haloperidol). There were no significant differences between standard and non-standard antipsychotic drugs. There were relations between duration of follow-up and risperidone.

Conclusions: Our results suggest that the choice of antipsychotic drug influences adherence to treatment. We need to examine the factors that affect the adherence to antipsychotics in more detail, to produce a better treatment outcome.

References:

1. Tognoni et al : Pharmacoepidemiology of psychotropic drugs in patients with severe mental disorders in Italy. Eur J Pharmacol 1999; 55: 685-690.
2. Kwon et al : Drug prescribing patterns of Outpatients with Schizophrenia in a University Hospital. J Korean Neuropsychiatr Assoc 2003; 42:683-690.

NR589 Tuesday, May 23, 3:00 PM - 5:00 PM

RNA Concentration in Postmortem Human Brain Tissue

Tatyana P. Shteinlukht, M.D. *UMass Medical School/UMMHC, Psychiatry, 151 Gerry Road, Chestnut Hill, MA, 02467-3185*, David A. Drachman, M.D., Jack Leonard, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that postmortem human brain tissue contains enough RNA to allow analysis of gene transcript levels. Such analysis is a valuable tool in studying psychiatric diseases.

Summary:

Objective: Analysis of gene transcript levels in postmortem human brain is a valuable tool in studying psychiatric diseases. RNA extraction and cDNA generation are important steps in this process. Since postmortem human brain tissue yields less RNA than many other human tissues the goal of the study was to clarify whether there is a sufficient amount of total RNA in postmortem human brain to allow cDNA generation.

Method: Stratagene Absolutely RNA Microprep Kit was used for RNA isolation from cells from previously frozen at -86°C postmortem human brain tissue. Quantitative and qualitative RNA analysis was done by measuring optical density of small sample diluted in 10 mM Tris, pH 7.5 at 260 nm and 280 nm. Ambion Message Sensor RT Kit RT-RCR was used for the cDNA synthesis and amplification in One Step RT-PCR reaction (40 PCR cycles). Human Actin Primers, M-MLV RT and Ambion SuperTaq polymerase were used. 1.4% Agarose Gel Electrophoresis was used to separate RCR products.

Results: Total RNA concentration in previously frozen at -86°C postmortem human brain tissue was 200-400 ng/mg of frozen tissue.

Conclusions: Previously frozen at -86°C postmortem human brain tissue contains enough total RNA to allow analysis of gene transcript levels.

References:

1. Li C, Wong WH: Model-based analysis of oligonucleotide arrays: expression index computation and outlier detection. Proc Natl Acad Sci U S A 2001; 98:31-36.

2. Pongrac J, Middleton FA, Lewis DA, Levitt P, Mirnics K: Gene expression profiling with DNA microarrays: advancing our understanding of psychiatric disorders. Neurochem Res 2002; 27:1049-1063.

NR590 Tuesday, May 23, 3:00 PM - 5:00 PM

Treatment of Tardive Dyskinesia With Vitamin E

Tatyana P. Shteinlukht, M.D. *UMass Medical School/UMMHC, Psychiatry, 151 Gerry Road, Chestnut Hill, MA, 02467-3185*

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize benefits of treatment of tardive dyskinesia (TD) with Vitamin E.

Summary:

Objective: To evaluate if Vitamin E is effective in treatment of neuroleptic-induced tardive dyskinesia (TD).

Method: 12 patients with TD were studied at the outpatient community clinic in open label fashion. Patients received the same dose and preparation of neuroleptic for at least 3 months prior to initiation of Vitamin E 400 IU PO 4 times a day and in the course of treatment. Abnormal Involuntary Movement Scale (AIMS) scores were checked at every visit (usually once a month). Treatment lasted 3 - 30 months. End point of treatment defined as 0 on AIMS scale or end of follow up by investigator. Data was analyzed using t-test.

Results: Results for up to 30 months duration of treatment are reported for the first time. Patients reported no side effects to Vitamin E. Reduction of AIMS scores from 5.16 + 1.13 to 1.00 + 0.50 (on average by 84.75%) with p<0,01 was noted. Patients who were more resistive to treatment had longer duration of antipsychotic therapy and were all elderly females except one.

Conclusions: Findings support the results of the majority of the prior studies. Vitamin E seems to be a viable treatment for such a disabling condition as TD.

References:

1. Adler LA, Rotrosen J, Edişon R, et al: Vitamin E for tardive dyskinesia. Arch Gen Psychiatry 1999; 56:836-841.

2. . Gupta S, Mosnik D, Black DW et al: Tardive dyskinesia: Review of treatments past, present and future. Ann Clin Psych 1999; 11(4):257-266.

NR591 Tuesday, May 23, 3:00 PM - 5:00 PM

Antidepressant Use in Iceland: Nationwide Population-Based Survey

Engilbert Sigurdsson, M.D. *Landspitali University Hospital, Psychiatry, Hringbraut, Reykjavik, 101, Iceland*, Thordis Olafsdottir, Pharm.D., Magnus Gottfredsson, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be aware that (1) by far the strongest indicator of willingness to use antidepressants for the treatment of depression was previous experience as users among 18-80 year-old adults in Iceland, (2) the more knowledgeable subjects were about antidepressants, the more positively they regarded their use in the treatment of depression, (3) since depression is often a relapsing-remitting disorder and indications for antidepressants expanding, sales in Iceland and elsewhere are likely to continue to rise still, (4) in light of the results of this nationwide population-based survey, this trend should perhaps cause less concerns at the Icelandic State Social Security Institute in the near future unless cheaper or more cost-effective treatment options become available.

Summary:

Background: Antidepressant sales have risen from 8 Defined Daily Doses (DDD) per 1000 Icelanders in 1975 to 95 DDD/1000 in 2005 which is higher than in any other European population that we are aware of. The State Social Security Institute (SSSI) pays around 60% of the cost. While the SSSI has repeatedly criticised this increase, little has been known about the views of members of the public on the effectiveness of antidepressants and about the factors that influence their views. Many users have complained about feeling guilty about using up valuable resources by using these widely prescribed drugs.

Methods: We devised a questionnaire in three parts to examine demographic factors, views and knowledge about antidepressant use and effectiveness. The questionnaire was sent to a randomly drawn sample of 2000 Icelanders 18-80 years of age.

Results: The 945 responders (47%) did not differ from non-responders by sex, age, education or residence. Around 8% (95%CI 6.2-9.6) were receiving antidepressants at the time of the survey and the same proportion had previously been on antidepressants for at least 6 weeks. Seven out of ten were willing to accept antidepressants as a treatment for depression. By far the strongest indicator of this was prior own experience of using antidepressants (OR 6.9, 95%CI 3.4-13.8), followed by knowing someone well who had been treated with antidepressants (OR 2.3, 95%CI 1.6-3.3). More than 3 out of every 4 (77%) who had used antidepressants felt that the benefits of therapy had outweighed the disadvantages. The more knowledgeable subjects were about antidepressants, the more likely they were to be willing to use them.

Conclusion: The majority of adult Icelanders are willing to use antidepressants for depression. The factors influencing their views most strongly are subjects' own experience of using them and the experience of close friends or relatives.

References:

1. Helgason T, Tómasson H, Zoéga T. Antidepressants and public health in Iceland. Time series analysis of national data. Br J Psychiatry 2004; 184:157-62.

2. Simon GE, Fleck M, Lucas R and Bushnell DM, M.A. LIDO Group. Prevalence and Predictors of Depression Treatment in an International Primary Care Study. Am J Psychiatry 2004;161:1626-1634.

NR592 Tuesday, May 23, 3:00 PM - 5:00 PM

Cardiovascular Effects of Extended-Release Dexmethylphenidate in Adults With ADHD and Hypertension

Thomas J. Spencer *Mass General Hospital, 55 Fruit Street. Warren 705, Boston, MA, 02114*, Lenard A. Adler, Timothy E. Wilens, Linda Pestreich, James Wang, Rafael Muniz

Educational Objectives:

At the end of this presentation, the attendee should be able to:

Understand the effects of d-MPH-ER on SBP/DBP and HR in patients with hypertension and ADHD.

Compare vital sign changes across d-MPH-ER doses in this population.

Summary:

Objectives: Some ADHD treatments have the potential to produce unwanted changes in vital signs in hypertensive patients. This analysis examined vital sign changes in adults receiving extended-release dexmethylphenidate (d-MPH-ER) 20-40 mg or placebo for 5 weeks.

Methods: Systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR) were measured in adults (18-60 years old) with DSM-IV-defined ADHD who took antihypertensive

medication or had hypertension reported as an adverse event (AE) during 5 weeks of double-blind treatment with d-MPH-ER doses of 20 (n=58), 30 (n=55), or 40 (n=55) mg/day, or placebo (n=53). Patients were started on 10 mg/day and titrated to their target dose at weekly intervals.

Results: Overall, 3 patients receiving d-MPH-ER 20 mg/day, 3 receiving 30 mg/day, and 5 receiving 40 mg/day took antihypertensive medication or had hypertension as an AE versus 1 patient receiving placebo. At baseline, mean SBP/DBP values for these patients were 140/92.3,140/82.3, 129.2/88.4, and 138/80.0 mm Hg, respectively. Respective values at end point were 135/85.0, 147/88.3, 127/87.2, and 120/84.0 mm Hg. At baseline, respective HR values were 70.7, 86.0, 73.2, and 80.0 bpm, and at end point, they were 65.3, 82.7, 71.4, and 80.0 bpm. No change from baseline in vital signs was statistically significant.**Conclusions:** In this small sample, d-MPH-ER did not adversely affect SBP/DBP or HR in patients taking antihypertensive medications or who had hypertension reported as an AE during treatment. The largest change was an 18-point drop in SBP, occurring in a placebo-treated patient.

References:

1. Adler LA, Spencer TJ, Milton DR, Moore RJ, Michelson D. Long-term, open-label study of the safety and efficacy of atomoxetine in adults with attention-deficit/hyperactivity disorder: an interim analysis. J Clin Psychiatry. 2005;66:294-299.
2. Wilens TE, Hammerness PG, Biederman J, et al. Blood pressure changes associated with medication treatment of adults with attention-deficit/hyperactivity disorder. J Clin Psychiatry. 2005;66:253-259.

NR593 Tuesday, May 23, 3:00 PM - 5:00 PM

Long-Term Effects of Extended-Release Dexmethylphenidate on Hemodynamic Variables and Body Weight in Adults With ADHD

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Educational Objectives:

Relatively little is known about the long-term effects of d-MPH-ER on hemodynamic variables and body weight in adult patients with ADHD. At the end of this presentation, the attendee should be able to:

Understand the changes in vital signs and weight observed over 6 months of treatment with d-MPH-ER.Describe cardiovascular adverse events reported in this open-label study of adults treated with d-MPH-ER.

Summary:

Objectives: Some ADHD medications may adversely affect hemodynamic variables and body weight with long-term treatment. This analysis examined changes in vital signs and body weight in adults receiving open-label extended-release dexmethylphenidate (d-MPH-ER) for 6 months.

Methods: One hundred seventy adult outpatients with DSM-IV-defined ADHD received d-MPH-ER starting at 10 mg/day, then flexibly titrated to 20-40 mg/day. Results were analyzed separately for patients who received mean d-MPH-ER doses ≤20, >20-30, and >30 mg/day.

Results: Mean baseline systolic/diastolic blood pressure for the ≤20, >20-30, and >30 mg/day groups were 118.0/75.0, 124.8/77.0, and 122.0/77.4 mm Hg, respectively. End point values were 121.2/75.0, 125.9/78.1, and 125.2/80.7 mm Hg. Baseline heart rate for the 3 groups were 71.2, 73.9, and 73.0 bpm, respectively, and 72.9, 75.7, and 79.8 bpm at end point. On average, patients were slightly overweight at baseline: 82.2, 88.2, and 92.9 kg. End point weights were 81.2, 87.7, and 89.4 kg. Significant decreases (≥7%) in weight occurred in 7.3%, 17.2%, and 29.2% of patients in the ≤20, >20-30, and >30 mg/day dosing groups. One patient discontinued d-MPH-ER because of palpitations and 2 discontinued because of tachycardia. One had a clinically relevant electrocardiographic abnormality at end point.

Conclusions: Long-term d-MPH-ER results in modest increases in

systolic/diastolic blood pressure, small increases in heart rate, and decreases

in weight that are greater with doses >30 mg/day.

References:

1. Rapport MD, Moffitt C. Attention deficit/hyperactivity disorder and methylphenidate. A review of height/weight, cardiovascular, and somatic complaint side effects. Clin Psychol Rev. 2002;22:1107-1131.
2. Wilens TE, Hammerness PG, Biederman J, et al. Blood pressure changes associated with medication treatment of adults with attention-deficit/hyperactivity disorder. J Clin Psychiatry. 2005;66:253-259.

NR594 Tuesday, May 23, 3:00 PM - 5:00 PM

The Effectiveness of Olanzapine Versus Divalproex in Clinical Practice: A One-Year Study of the Treatment of Mixed, Manic, and Hypomanic Episodes of Bipolar Disorder

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Educational Objectives:

At the end of the presentation, attendees will understand differences in long-term clinical outcomes for patients with bipolar disorder treated with olanzapine or divalproex in typical clinical practice.

Summary:

Objective: To compare outcomes for individuals with bipolar disorder treated with olanzapine or divalproex in usual clinical practice without entry criteria and treatment intervention constraints of randomized, controlled trials.

Method: 363 adults with SCID diagnosed bipolar disorder in a hypomanic, manic, or mixed episode initiating on either olanzapine (N = 179) or divalproex (N=184) were followed 1 year. Patients from 31 U.S. sites were assessed at enrollment, 3 weeks, 3 months, 6 months, and 12 months with the Young Mania Rating Scale (YMRS), Montgomery-Asberg Depression Rating Scale (MADRS), and Clinical Global Impression (CGI)-Severity scale. Propensity scores were used to correct for selection bias from non-randomization. Marginal Structural Models were used to compare outcomes.

Results: Similar proportions of olanzapine (35.2%) and divalproex (34.2%) patients remained on initial medication for the full year. YMRS score decreased more in olanzapine than divalproex treated patients over 1 year (p = .026). Visit-wise treatment differences were non-significant at 3-weeks but statistically significant at 12 months (p = .043). Olanzapine treated patients had greater improvement on CGI (p = .041) but not MADRS. **Conclusion:** In an observational study of usual clinical practice, olanzapine versus divalproex treated bipolar patients had greater long-term manic symptom improvement.

References:

1. Tohen M, Ketter TA, Zarate CA, et al. Olanzapine versus divalproex sodium for the treatment of acute mania and maintenance of remission: a 47-week study. Am J Psychiatry. 2003;160:1263-1271.

2. Roy-Byrne PP, Sherbourne CD, Craske MG, et al. Moving treatment research from clinical trials to the real world. Psychiatr Serv. 2003;54:327-332.

NR595 Tuesday, May 23, 3:00 PM - 5:00 PM

Association Between Atypical Antipsychotic Compliance and Hospitalization and Emergency Department Visits in Patients With Bipolar Disorder

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Educational Objectives:

At the end of this presentation, the participant should have gained knowledge of: 1) the evaluation of compliance using the medication possession ratio; and 2) the association between compliance with atypical antipsychotics and the likelihood of hospitalization and emergency department visits in patients with bipolar disorder.

Summary:

Objectives: Determine the association between compliance with atypical antipsychotics (AA) and likelihood of hospitalizations and emergency department (ED) visits among patients with bipolar disorder (BPD).

Methods: Retrospective analysis of 2,785 patients with BPD in a US multi-managed care plan database (2000-2004; PharMetrics). Compliance was assessed with the medication possession ratio (MPR): ratio of days of possession of any AA during the first year of follow-up to days of follow-up in the first year after the first prescription of an AA. Cut-off levels for compliance were MPR≥0.80 and MPR value ≥80th percentile. Statistical analysis was undertaken using logistic regression modeling.

Results: 16.8% (N=467) had MPR≥0.80 and 19.9% (N=554) had MPR≥80th percentile (0.758) for any AA. More compliant patients (MPR≥0.80) had significantly fewer hospitalizations or ED visits than less compliant patients during one year of follow-up (51.2% versus 58.0%, *P*=0.007). Hospitalizations or ED visits were similarly lower in more compliant patients based on MPR≥80th percentile (52.7% versus 57.9%, *P*=0.028). More compliant patients were less likely to have a hospitalization or ED visit in the first year of follow-up than less compliant patients (MPR≥0.80: OR=0.75, CI 0.60-0.92; MPR≥80th percentile: OR=0.80, CI 0.65-0.98).**Conclusion:** Increased compliance with AA was associated with a decreased risk of hospitalization or ED visits among patients with BPD in the first year of follow-up.

Supported by funding from AstraZeneca Pharmaceuticals LP.

References:

1. Eaddy, M., Grogg, A., Locklear, J. (2005) Assessment of compliance with antipsychotic treatment and resource utilization in a Medicaid population. Clin Ther 27:263-72.

2. Svarstad, B.L., Shireman, T.I., Sweeney, J.K. (2001) Using drug claims data to assess the relationship of medication adherence with hospitalization and costs. Psychiatr Serv 52:805-11.

NR596 Tuesday, May 23, 3:00 PM - 5:00 PM

Quetiapine in Patients With Schizophrenia and Substance Use Disorder

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Educational Objectives:

At the conclusion of this presentation, the participant should understand the advantages of using quetiapine in patients with schizophrenia and substance use disorders

Summary:

Objective: Evidence suggests that atypical antipsychotics,[1] including quetiapine,[2] can relieve substance craving in patients with schizophrenia. This open-label study investigated quetiapine treatment in patients with substance use disorder (SUD) and schizophrenia.

Methods: Twenty-nine patients with a schizophrenia spectrum disorder (DSM-IV) and comorbid SUD (abuse or dependence; ≥3 months) were switched from previous antipsychotics to quetiapine (200-800 mg/day) for 12 weeks. Efficacy measures, including SUD severity (Alcohol Use and Drug Use Scales), craving for drug of choice (modified Penn Alcohol Craving Scale [mPACS]) and quantities of psychoactive substances (PAS) used (measured by money spent) were assessed at weeks 3, 6, 9 and 12 (ANOVA for repeated measures performed). PANSS, CDSS and EPS Rating Scale scores were also assessed.

Results: Twenty-four patients completed the study; patients were switched from one or more of olanzapine (n=15); risperidone (n=5), ziprasidone (n=1), haloperidol (n=3) or conventional antipsychotics (n=4). Patients had ≥1 SUD: cannabis only (n=10); alcohol only (n=5); PAS only (n=1); cannabis+alcohol (n=1); alcohol+PAS (n=3); cannabis+PAS (n=4). At endpoint (LOCF), quetiapine treatment (mean dose 545.8 mg/day; mean duration 11.9 weeks) caused a significant reduction in SUD severity ($p<0.01$) and PAS use ($p<0.01$). Cannabis (but not alcohol) cravings decreased significantly (mPACS; $p<0.01$). PANSS ($p<0.01$), CDSS ($p<0.01$) and EPS Rating Scale ($p<0.05$) scores were significantly improved.

Conclusions: Quetiapine treatment significantly improved SUD, psychiatric and depressive symptoms, and EPS in patients with schizophrenia.

References:

1. Zimmet SV, Strous RD, Burgess ES, Kohnstamm S, Green AI: Effects of clozapine on substance abuse in patients with schizophrenia and schizoaffective disorder: a retrospective survey. J Clin Psychopharmacol 2000; 20:94-98.

2. Weisman RL: Quetiapine in the successful treatment of schizophrenia with comorbid alcohol and drug dependence: a case report. Int J Psychiatry Med 2003; 83:85-89.

NR597 Tuesday, May 23, 3:00 PM - 5:00 PM

Psychosocial Impact, Work and Legal Complications Among Antidepressant Nonresponders Who Screen Positive for Bipolar Disorder

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Educational Objectives:

To better understand the psychosocial and work-related impact and legal complications among patients with depression who are at risk for bipolar disorder.

Summary:

Educational Objective: To better understand the psychosocial and work-related impact and legal complications among patients with depression who are at risk for bipolar disorder.

Objective: To assess impairment associated with undetected for bipolar disorder (BPD) among patients currently in treatment for unipolar depression.

Method: Psychiatrists from community and private practice clinic settings randomly selected patients with unipolar depression that have failed one or more antidepressant (AD) medication trials. Patients with a prior diagnosis of BPD, OCD, or schizophrenia were excluded. Patients who screened positive on the Mood Disorder Questionnaire (MDQ) were considered "undetected" BPD. Medical record abstraction obtained patient history as well as current and prior AD medication use. A self-administered survey collected patient demographics, Quality of Life Enjoyment and Satisfaction data (QLESQ-SF), work and social and family life disruption via Sheehan Disability Scale (SDS), work impairment via Work and Social Adjustment Scale (WSAS) and legal complications via the legal status section of the Addiction Severity Index (Legal).

Results: Data were collected from 602 patients. A total of 18.6% (112 patients) were MDQ positive. Compared with MDQ negative patients, MDQ positive patients had lower QLESQ-SF ($F=3.7$, $p<.055$), more SDS disruption in work ($F=6.5$, $p<.011$) social ($F=8.2$, $p<.004$) and family ($F=12.1$, $p<.001$) domains, more WSAS work impairment ($F=14.4$, $p<.0001$) and more Legal complications ($chi=9.2$, $p<.002$).

Conclusions: These findings suggest that depression patients with undetected BPD were impaired in a variety of functional areas and should be carefully evaluated for BPD so that appropriate treatments can be offered.

Research supported by GlaxoSmithKline.

References:

1. Calabrese JR, Hirschfeld RM, Reed M, Davies MA, Frye MA, Keck PE, Lewis L, McElroy SL, McNulty JP, Wagner KD. Impact of bipolar disorder on a U.S. community sample. J Clin Psychiatry. 2003 Apr;64(4):425-32.
2. Hirschfeld RM, Lewis L, Vornik LA. Perceptions and impact of bipolar disorder: how far have we really come? Results of the national depressive and manic-depressive association 2000.

NR598 Tuesday, May 23, 3:00 PM - 5:00 PM

Divalproex Use and Utility in a Prison Population

Humberto Temporini, M.D. *University of Connecticut School of Medicine, Psychiatry, 263 Farmington Avenue, Farmington, CT, 06030-1410*, Susan Quarti, M.S., Wanli Zang, Ph.D., Karen Pagano, M.S., Nicholas Demartinis, M.D., Robert L. Trestman, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize common uses for divalproex in a correctional setting, as well as discuss its efficacy in this population.

Summary:

This retrospective review of divalproex use in the Connecticut Department of Correction examined the psychiatric diagnoses of patients receiving divalproex, doses used, and symptomatic/functional change over time. *Methods:* Inmates receiving divalproex for > one month between January 2002 through March 2003 were eligible. 150 male and 50 female charts were randomly selected for review out of 961 eligible charts. *Results:* The most common Axis I diagnoses in inmates receving divalproex were: bipolar disorder (54.8%), polysubstance abuse/dependence (51.2%), MDD (13.7%), schizoaffective disorder (8.9%), posttraumatic stress disorder (7.1%) and schizophrenia (6.5%). 55.4% of the inmates met criteria for two axis I disorders, 7.7% met criteria for three and 1.8% for four. 25% of the sample had an Axis II diagnosis; the most common being BPD (13.7% of sample) and antisocial personality disorder (13.1%). The duration of treatment with divalproex ranged from 0.72 to 37.25 months (mean, 7.49). Overall, 52% of the sample was assessed as having improved clinically with treatment, 33% was unchanged, and 13.7% showed deterioration. Dose was not correlated with clinical change. *Conclusions:* Divalproex is commonly prescribed in correctional settings for a wide range of Axis I and II disorders, and is associated with clinical improvement.

References:

1. Bowden CL, Singh V. Valproate in bipolar disorder: 2000 onwards. Acta Psychiatr Scand Suppl. 2005;(426):13-20.
2. Davis LL, Ryan W, Adinoff B, Petty F.Comprehensive review of the psychiatric uses of valproate.J Clin Psychopharmacol. 2000 Feb;20(1 Suppl 1):1S-17S.

NR599 Tuesday, May 23, 3:00 PM - 5:00 PM

Biological Mechanisms Involved in the Modification of the Membrane Phospholipidic Asymmetrical Distribution in RBC Membranes From Schizophrenic Patients: Putative Role of the Aminophospholipidic Transporters

Cédric Tessier *INSERMU538, 27 rue de Chaligny, Paris, 75012, France*, Philippe Nuss, Florian Ferreri, Germain Trugnan

Educational Objectives:

A significant decrease in the asymmetrical PE (phosphatidylethanolamine) gradient in erythrocyte membranes has been found in 2/3 of schizophrenic patients (G1) as compared to healthy controls (G0). The mean ratio between external/internal PE in RBC membranes from healthy controls is 4/96 whereas in this G1 group this ratio is significantly ($p< 0.05$) higher: 8/92. We wanted to study the phospholipid membrane transporters activities in the erythrocyte membranes from the a group of schizophrenic patients with membrane abnormality (G1) versus schizophrenic patients without the abnormality (G2) and healthy controls (G0).

Summary:

Method: RBC from schizophrenic patients and healthy controls were isolated after blood puncture ($n_1=3$ from patients from the G1 group, $n_2=3$ from the G2 group and $n_3=3$ from the G0 group)

We studied in Extended Release ythrocytes ghost (made with membranes from n_1, n_2, n_3) the PE/PS kinetic internalization process with labelled PE/PS. The ATP concentration was concomitantly assessed.**Results:** The APLT activity in RBC membranes from the G1 group compared to G2 and G0 groups is following a distinct activation pattern. The PE asymmetrical distribution results from a complex mechanism, involving several transporters and not only, as initially hypothesise a decreased activity of the APLT.

References:

1. Devaux PF. Protein involvement in transmembrane lipid asymmetry. Annu Rev Biophys Biomol Struct. 1992;21:417-39.
2. Fellmann P, Herve P, Pomorski T, Muller P, Geldwerth D, Herrmann A, Devaux PF. Transmembrane movement of diether phospholipids in human erythrocytes and human fibroblasts. Biochemistry. 2000 May 2;39(17):4994-5003.

NR600 Tuesday, May 23, 3:00 PM - 5:00 PM

Efficacy of Quetiapine Monotherapy in Bipolar Depression: A Confirmatory Double-Blind, Placebo-Controlled Study (The BOLDER II Study)

Michael E. Thase, M.D. *University of Pittsburgh Medical Center, Department of Psychiatry, Western Psychiatric Institute*

and Clinic, 3811 O'Hara Street, Pittsburgh, PA, 15213-2593, Robin McCoy, William Chang, Wayne Macfadden, M.D.

Educational Objectives:

At the conclusion of this session, the participants will be able to: 1) evaluate the recent data on efficacy and tolerability of quetiapine for bipolar depression and 2) use this information in the management of patients with bipolar disorder.

Summary:

Objective: To evaluate the efficacy and tolerability of quetiapine monotherapy for depressive episodes in patients with bipolar disorder.[1,2]

Methods: Patients with bipolar I or II depression (DSM-IV) were randomized to 8 weeks of double-blind treatment with quetiapine (300 or 600 mg/d; once-daily, evening dosing) or placebo. Patients were assessed weekly using MADRS and HAM-D. The primary endpoint was change in MADRS total score from baseline to Week 8 (ANCOVA/LOCF analysis).

Results: Of 509 patients randomized, 59% completed the study. Improvements from baseline in mean MADRS total scores were significantly greater with quetiapine 300 and 600 mg/d than with placebo from first evaluation, Week 1 (change from baseline with quetiapine 300 and 600 mg/d: -9.42 and -9.14, respectively; both $P<0.001$ versus placebo: -6.10) through to Week 8 (change from baseline with quetiapine 300 and 600 mg/d: -16.94 and -16.00 respectively; both $P<0.001$ versus placebo: -10.2). MADRS effect sizes at Week 8 were 0.54 and 0.61 for quetiapine 300 and 600 mg/d, respectively. Improvements in mean HAM-D scores were also significantly greater with both quetiapine doses than with placebo ($P<0.001$) throughout the study (Week 8 effect sizes 0.61 and 0.55 for 300 and 600 mg/d, respectively). There were significant improvements in primary and secondary outcomes with both 300 and 600 mg/d quetiapine, without major differences in the doses. Common AEs included dry mouth (300 mg/d: 42.7%, 600 mg/d: 47.0%, placebo: 18.0%), sedation (32.2%, 27.4%, 10.2%), somnolence (29.8%, 29.8%, 4.8%), and dizziness (14.0%, 16.1%, 5.4%). Generally, AEs were mild in intensity, discontinuation rates due to AEs were 8.1% (300 mg/d), 11.2% (600 mg/d), and 1.2% (placebo).

Conclusions: These results replicate those of the BOLDER I study[2] and confirm that quetiapine monotherapy is an effective and well-tolerated treatment for depressive episodes in bipolar disorder.

Supported by funding from AstraZeneca Pharmaceuticals LP.

References:

1. Post RM, Leverich GS, Altshuler LL, Frye MA, Suppes TM, Keck PE, et al. An overview of recent findings of the Stanley Foundation Bipolar Network (Part I). Bipolar Disord 2003;5(5):310-19.
2. Calabrese JR, Keck PE, Jr., Macfadden W, Minkwitz M, Ketter TA, Weisler RH, et al. A randomized, double-blind, placebo-controlled trial of quetiapine in the treatment of bipolar I or II depression. Am J Psychiatry 2005;162(7):1351-60.

NR601 Tuesday, May 23, 3:00 PM - 5:00 PM

Olanzapine/Fluoxetine Combination, Olanzapine, and Fluoxetine in Treatment-Resistant Major Depressive Disorder

Michael E. Thase, M.D. *University of Pittsburgh Medical Center, 3811 O'Hara Street, Pittsburgh, PA, 152132593*, Sara A. Corya, M.D., Olawale Osuntokun, M.D., Todd M. Sanger, Ph.D., Michael Case, M.S., Susan B. Watson, Ph.D., Sanjay Dube, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to describe the acute efficacy and safety profile of olanzapine/fluoxetine combination in treatment-resistant depression.

Summary:

Objective. The olanzapine/fluoxetine combination (OFC) has been previously reported as effective in treatment-resistant depression.[1,2] Two parallel 8-week double-blind studies compared OFC, olanzapine (OLZ), and fluoxetine (FLX) in TRD.

Methods. TRD was defined as current episode SSRI failure and prospective fluoxetine failure. 605 nonresponders during an 8-week fluoxetine lead-in phase were randomized to OFC, OLZ, or FLX. Efficacy was evaluated with the MADRS. Data were analyzed via mixed-effects model repeated measures analysis of variance.

Results. After 8 weeks of double-blind treatment, pooled results (studies 1 and 2 combined) revealed that OFC patients demonstrated significantly greater MADRS improvement (-12.7) than FLX (-9.0, $p<.001$) and OLZ (-8.8, $p<.001$) patients. Response rates were 40% for OFC, 30% for FLX, and 26% for OLZ. Adverse events in ≥10% of OFC patients were weight gain, increased appetite, dry mouth, somnolence, fatigue, headache, peripheral edema, hypersomnia, and tremor. Cholesterol mean change (mg/dL) was +15.1 for OFC, +0.8 for FLX, and +2.7 for OLZ. Mean weight change (kg) was +4.9 for OFC, +0.4 for FLX, and +5.5 for OLZ.

Conclusions. Pooled results revealed that OFC patients demonstrated significantly greater improvement in depressive symptoms than those taking OLZ or FLX alone.

References:

1. Corya SA, Williamson D, Sanger TM, Briggs SD, Case M, Tollefson GD. A randomized, double-blind comparison of olanzapine/fluoxetine combination, olanzapine, fluoxetine, and venlafaxine in treatment-resistant depression. Depress Anxiety, in press.
2. Shelton RC, Williamson D, Corya SA, Sanger T, Van Campen LE, Case M, Briggs SD, Tollefson GD. Olanzapine/fluoxetine combination for treatment-resistant depression: a controlled study of SSRI- and nortripyline resistance. J Clin Psychiatry 2005, 66:12.

NR602 Tuesday, May 23, 3:00 PM - 5:00 PM

Pooled Analysis of Remission Rates Following Monotherapy With Bupropion or a Selective Serotonin Reuptake Inhibitor: Impact of Additional Data

Michael E. Thase, M.D. *University of Pittsburgh Medical Center, Psychiatry, 3811 O'Hara Street, Pittsburgh, PA, 152132593*, Barbara Haight, Pharm.D., Nathalie E. Richard, M.S., Alok Krishen, M.S., Anne Andorn, M.D.

Educational Objectives:

At the end of this presentation the participant will be familiar with the newer meta-analysis of remission rates during treatment with bupropion or an SSRI from recently completed studies.

Summary:

Background: Remission is widely believed to be the best criterion by which to compare the efficacy of antidepressants. A previous meta-analysis demonstrated that bupropion has remission rates comparable to SSRIs in MDD. We hypothesized that this finding would not be changed by including new additional data sets.

Objective: We now report a further meta-analysis of remission rates during treatment with bupropion or an SSRI including data

from two recently-completed studies comparing bupropion and the SSRI escitalopram.

Methods: Data were pooled from 9 randomized, double-blind, acute-phase studies of MDD. Patients received bupropion XL 300-450mg/day (n=276), bupropion Sustained Release 100-400mg/day (n=688), bupropion IR 225-450mg/day (n=60), escitalopram 10-20mg/day (n=281), fluoxetine 20-60mg/day (n=348), sertraline 50-200mg/day (n=358), paroxetine 10-40mg/day (n=52) or placebo (n=797). Remission rates (17-item Hamilton Rating Scale for Depression score ≤7) were calculated at week 8 or endpoint using pooled data from all 9 studies and separately for the 6 studies that included a placebo control.

Results: Remission rates for the analysis of all studies were 46% for bupropion, 46.8% for SSRIs and 35.5% for placebo (statistical equivalence within 5%). Remission rates for both active treatments were superior to placebo (p<0.001). For the subset of studies that included a placebo control, remission rates were 44% for bupropion, 45% for SSRIs and 36% for placebo (p<0.001 bupropion and SSRIs v. placebo). The five active treatments were well tolerated and showed similar overall frequencies of adverse events. However, the SSRIs, including escitalopram, were associated with a greater incidence of orgasm dysfunction, sexual arousal disorder, and sexual desire disorder compared to bupropion and placebo.

Conclusions: Bupropion monotherapy produced similar remission rates as the SSRIs. All medications were well-tolerated; however, SSRI therapy resulted in higher rates of sexual dysfunction compared to bupropion and placebo.

References:

1. Thase ME, et al: Remission rates following antidepressant therapy with bupropion or selective serotonin reuptake inhibitors: a pooled analysis of original data from seven randomized controlled trials. J Clin Psychiatry 2005; 66(8):974-981.
2. Fava M, Rush AJ, Thase ME, Clayton A, Stahl SM, Pradko JF, Johnston JA. Bupropion HCl: 15 years of clinical experience. Prim. Care Companion J Clin Psychiatry 2005; 7(3):106-113.

NR603 Tuesday, May 23, 3:00 PM - 5:00 PM

Predicting Remission in Depressed Outpatients Treated With Venlafaxine Extended Release (XR) or Selective Serotonin Reuptake Inhibitors (SSRI) by Examining Symptom Improvement Patterns

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Educational Objectives:

1. At the conclusion of this presentation, the participant should be able to assess how symptom improvements may be used to predict remission in major depression.
2. At the conclusion of this presentation, the participant should be able to evaluate how differing patterns of symptom improvement may help to predict which patients will achieve remission on which class of antidepressant.
3. At the conclusion of this presentation, the participant should be able to discuss the different symptom domains in major depression.

Summary:

Objective: Subanalysis of a 180-day, open-label study to assess patterns of symptom improvement and remission in the first 4 weeks of treatment.

Methods: MDD outpatients (N=1385) with a HAM-D_{17} total score ≥20 were randomly assigned to receive venlafaxine XR (n=688) or an SSRI (n=697). Remission rates (HAM-D_{17} total score ≤7) for venlafaxine XR and SSRIs were compared at 90 and 180 days. Patient change scores for the mood, psychic anxiety, somatic, and combined anxiety and somatic symptom domains during baseline to day 14, day 14 to 30, and baseline to day 30 treatment periods were compared with remission status at day 90 and 180.

Results: Remission rates at day 90 were 35.0% (193/552) and 29.5% (163/553) for venlafaxine XR and SSRIs, respectively. Predictors that best distinguish remitters and nonremitters (at day 90) for venlafaxine XR-treated patients were the day 14 to 30 mood (P=0.0006) and somatic symptom (P=0.0005) domain change scores; the day 14 to 30 somatic (P=0.0052) domain change score was the best predictor for the SSRIs.

Conclusions: Although the pattern of symptom improvement was statistically significant in favor of venlafaxine versus SSRIs, this level of significance has not been evaluated for each individual SSRI. In this study, the pattern of symptom improvement differed significantly for the 2 treatment groups. These data may help to predict the patients who will achieve remission with which antidepressant agents.

References:

1. Szegedi A, et al: Early improvement under mirtazapine and paroxetine predicts later stable response and remission with high sensitivity in patients with major depression. J Clin Psychiatry 2003; 64:413-.
2. Trivedi MH, Morris DW, Grannemann BD, Mahadi S: Symptom clusters as predictors of late response to antidepressant treatment. J Clin Psychiatry. 2005;66:1064-1070.

NR604 Tuesday, May 23, 3:00 PM - 5:00 PM

Clinical Features of 35 % Carbon Dioxide Challenge Test in Panic Disorder: A Comparison With Spontaneous Panic Attacks

Alexandre Martins Valença, M.D. *Federal University of Rio de Janeiro, Laboratory of Panic and Respiration, R. da Cascata 13 apto 501-Tijuca - CEP 20530-080, Av. Venceslau Brás 71-Botafogo CEP 22290-000, Rio de Janeiro, 20530-080, Brazil,* Antonio Egidio Nardi, M.D., Isabella Nascimento, M.D., Rafael C. Freire, M.D., Marco A. Mezzasalma, M.D., Valfrido Melo, M.D., Fabiana L. Lopes, M.D.

Educational Objectives:

Our educational objective is to study the psychopatological profile of 35% carbon dioxide induced panic attacks

Summary:

Aim: to describe the clinical features of 35% carbon dioxide (CO2) induced panic attacks in panic disorder (PD) patients - DSM-IV - and compare them with the last spontaneous panic attack in PD patients who had not a panic attack after the 35% CO2 challenge test.

Method: We examined 91 PD patients submitted to the CO2 challenge test. The test consisted of exhaling as fully as possible, took a fast vital capacity breath, held their breath for 8 s, exhaled and then repeated the fast vital capacity breath, again holding for 8 s. The patients inhaled the 35% CO2 / 65% oxygen mixture or atmospheric compressed air, randomly selected in a double-blind design. Scales were applied before and after the test. A total of 68.1% (n=62) PD patients had a panic attack (responders) after the CO2 test (χ^2= 25.87, df= 1, p=0.031). The last spontaneous panic attack and the symptoms profile from the PD patients who had not a panic attack after the test (n= 29, 31.9%) were described to compare.

Results:The responders had more respiratory symptoms (χ^2= 19.21, df= 1, p<0.001), fullfiling the criteria for respiratory PD subtype (80.6%), the disorder started earlier (Mann-Whitney, p<0.001), had a higher familial prevalence of PD (χ^2= 20.45, df= 1, p=0.028), and had more previous depressive episodes (χ^2= 27.98, df= 1, p<0.001).

Conclusion: there is an association between respiratory PD subtype and hyperreactivity to a CO2 respiratory challenge test. The responders may be a sub-group of respiratory PD subtype with future diagnostic and therapeutic implications.

References:

1. Valença, AM, Nardi, AE, Nascimento, I, Zin, WA, Versiani, M. 2002. Respiratory panic disorder subtype and sensitivity to the carbon dioxide challenge test. Braz J Med Biol Res 35: 783-788.
2. Nardi, AE, Valença, AM, Lopes, FL, Nascimento, I, Mezzasalma, MA, Zin, WA. 2004. Clinical features of panic patients sensitive to hyperventilation or breath-holding methods for inducing panic attacks. Braz J Med Biol Res 37: 251-257.

NR605 Tuesday, May 23, 3:00 PM - 5:00 PM

Efficacy of Indiplon During the First Treatment Night in Studies of Primary Insomnia

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Educational Objectives:

The research data presented will contribute to the participant's understanding of the onset of efficacy of $GABA_A$ receptor modulators in the treatment of insomnia.

Summary:

Objective: To evaluate the efficacy of indiplon, a Gamma-aminobutyric acid $_A$ receptor modulator with selectivity for receptors with the α_1 sub-unit, during the first night of treatment.

Methods: Data were combined from 4 similarly designed studies (double-blind, placebo-controlled, outpatient trials with nightly treatment) evaluating the efficacy of indiplon in treating adults and elderly patients meeting DSM-IV criteria for primary insomnia. Treatment durations ranged from two weeks to three months. ANOVA was performed on patient self-assessments of latency to sleep onset (LSO, mins), sleep maintenance (wake time after sleep onset; WASO, mins), and total sleep time (TST, mins).

Results: Significantly shorter LSO (+ se) was observed on the first night of treatment with indiplon 5 mg (34.7 + 3.0), 10 mg (35.6 + 1.8), and 15 mg (26.3 + 1.6) versus placebo (45.7 + 1.8). Similarly, shorter WASO was observed on the first night of treatment with indiplon 5 mg (68.4 + 6.2), 10 mg (53.4 + 3.6), and 15 mg (54.2 + 4.4) versus placebo (74.2 + 2.8). Overall, TST was significantly longer on indiplon 5 mg (342.5 + 9.1), 10 mg (364.4 + 5.3), and 15 mg (378.4 + 6.4) versus placebo (326.5 + 4.2). First night efficacy was independent of clinical and demographic variables such as baseline insomnia severity, age, and gender.

Conclusions: Treatment with indiplon achieved rapid effects regardless of insomnia severity and these effects persisted throughout the study duration.

References:

1. Foster AC, Pelleymounter MA, Cullen MJ, Lewis D, Joppa M, Chen TK, Bozigian HP, Gross RS, Gogas KR. In vivo pharmacological characterization of indiplon, a novel pyrazolopyrimidine sedative-hypnotic. J Pharmacol Exp Ther 2004;311:547-559.
2. Simon GE, VonKorff M. Prevalence, burden, and treatment of insomnia in primary care. Am J Psychiatry 1997;154:1417-1423.

NR606 Tuesday, May 23, 3:00 PM - 5:00 PM

Effects of Variable Wear Times on Transdermal Methylphenidate in ADHD

Timothy E. Wilens, M.D. *Massachusetts General Hospital, 15 Parkman Street, WACC 725, Boston, MA, 02114,* Sharon B. Wigal, Ph.D., Howard Abikoff, Ph.D., Michael Manos, Ph.D., Sharon Reinhard, M.S., Tarra Shingler, M.S.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to: Describe the clinical use of the methylphenidate transdermal system (MTS) in pediatric subjects based on variable wear-times. Discuss ratings of efficacy and behavior as compared to placebo in the laboratory classroom environment.

Summary:

Objective: The methylphenidate transdermal system (MTS) may offer a flexible duration of action for the treatment of ADHD. This study was conducted to assess the efficacy and duration of effect of MTS compared with a placebo transdermal system (PTS) using 4- and 6-hour wear times during laboratory classroom sessions.

Method: This was a randomized, double-blind, placebo-controlled, 3-way crossover laboratory classroom study with a lead-in dose optimization phase. Children aged 6-12 years diagnosed with ADHD by DSM-IV-TR criteria were enrolled. The SKAMP-Deportment (behavior) was the primary behavioral outcome measure used in the classroom. Duration of effect was assessed using Permanent Product Measure of Performance (PERMP) age-adjusted math test scores. Additional efficacy measures included ADHD-RS-IV Rating Scale scores, and clinician and parent ratings.

Results: Mean SKAMP-D scores were significantly lower for both MTS 4- and 6-hour wear times, compared with placebo. Mean PERMP number of math problems attempted and number correct were significantly greater for both MTS wear times, compared with placebo. Overall, treatment with MTS resulted in a statistically significant (p<0.0001) mean change from baseline in ADHD-RS-IV scores at all visits compared with placebo.

Conclusion: Compared with placebo, treatment with MTS resulted in significant improvements in all outcome measures analyzed. MTS was generally well-tolerated and no serious side effects were reported. MTS may be an effective non-oral alternative treatment for pediatric ADHD, allowing flexibility in the duration of effect.

Supported by funding from Shire US Inc.

References:

1. Wigal S, McGough JJ, Abikoff H, Turnbow JM, Posner K, and Moon E. Behavioral effects of methylphenidate transdermal system in children with ADHD. Poster presented at the joint meeting of AACAP and CACAP. Toronto, Ontario. October 21, 2005.
2. Pierce DM, Dixon CM, Wigal SB, and McGough JJ. Pharmacokinetics of methylphenidate transdermal system in children with attention deficit/hyperactivity disorder. Poster presented at the joint meeting of AACAP and CACAP. Toronto, Ontario. Oct 20, 2005.

NR607 Tuesday, May 23, 3:00 PM - 5:00 PM

Combined OROS-Methylphenidate and Atomoxetine Treatment in Children With ADHD

Timothy E. Wilens, M.D. *Massachusetts General Hospital, Psychiatry, 55 Fruit Street, YAWKEY 6A, Boston, MA, 02114,* Paul Hammerness, M.D., Thomas J. Spencer, M.D., Julia Whitley, B.S., Stephanie Traina, B.A., Alison Santry, B.A., Joseph Biederman, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the efficacy of using both stimulants and non-stimulants to treat ADHD. In addition, the participant should be able to understand the tolerability issues surrounding treatment with both stimulants and non-stimulants.

Summary:

Objective: Despite the use of combined atomoxetine (ATMX) and stimulant, there are no prospectively collected data demonstrating either efficacy or tolerability of the combination. The aim of the study was to evaluate the efficacy and safety/tolerability of adding OROS-MPH (CONCERTA) to children who have had at least mild ADHD symptoms on ATMX for ADHD. Method: This is an ongoing, two-phase, 7-week open-label study in patients aged 6 to 17 years. Phase one initiates ATMX for a minimum of four weeks. Phase two enters ATMX partial responders and adds OROS-MPH to their regimen. Subjects are assessed on multiple outcomes including ADHD-RS (rating scale), executive functioning and adverse effects. Results: At midpoint, 33 subjects were exposed to ATMX and 22 subjects entered into Phase II. Overall, there was a 60% reduction in the ADHD-RS from pre-drug baseline to end of study. The addition of OROS-MPH to ATMX resulted in a 32% drop in ADHD symptoms ($p < 0.0001$). In addition, there were clinically significant reductions in CGI-Severity from moderate to mild ADHD (23%, $p < 0.0001$), improvements on CGI after Phase I (59%) and Phase II (67%), and improvements in executive functioning. There were no serious adverse events; however, side effects appear to be additive with headache, nausea, insomnia, appetite loss and lethargy most commonly reported on the combination. Conclusions: These preliminary results suggest that OROS MPH added to partial responders of ATMX improves ADHD and executive functioning and is well tolerated.

This research is supported by a grant from McNeil Consumer & Specialty Pharmaceuticals.

References:

1. Wilens, T, et al: Attention Deficit/Hyperactivity Disorder Across the Lifespan. Annual Review of Medicine 2002; 53: 113-131.
2. Brown, T: Atomoxetine and Stimulants in Combination for Treatment of ADHD: Four Case Reports. Journal of Child and Adolescent Psychiatry; 14(1): 129-36.

NR608 Tuesday, May 23, 3:00 PM - 5:00 PM

Association of G70/G30 Locus With Schizophrenia in the Korean Population

Sung-il Woo, M.D. *Soonchunhyang Univ. Hospital, Psychiatry, 657 Hannam Dong, Yongsan Gu, Seoul, 140-743, Republic of Korea,* Byung Lae Park, Ph.D., Hyun Sub Cheong, Hyoung Doo Shin, Chang Hee Lee, Jin-Wook Sohn, Sun-Ho Han

Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand that genetic variations in G72/G30 gene might have significant influence on the pathogenesis of schizophrenia in the Korean population.

Summary:

Aims : Recently, Chumakov et al. reported association of SNPs in G72 gene from 13q4 with schizophrenia. SNP markers M12, M14, M15, M22, M23 and M24 from G72 gene showed significant association with schizophrenia in the Canadian and Russian population. This finding was consistently replicated by other investigators in schizophrenic patients from various ethnic origins except one study by Mulle et al. The aim of this study was to investigate the association of eleven SNPs in G72 gene with schizophrenia in the Korean population.

Subjects and Methods : Eleven SNPs in G72/G30 were analyzed in 388 Patients with Schizophrenia and 367 normal controls from Korean population. Genotyping was done from DNAs by TaqMan assay. Logistic and chi-square analysis were used for statistical analysis..

Results : Significant differences in genotype frequency between patient and control groups were observed in five (M18, M19, M21, M22 and M23) of the eleven SNPs ($p=0.01\sim0.05$). Significant differences in allele frequency of M18, M19 and M21 were also observed ($p=0.03\sim0.008$). In haplotype association analysis, one common haplotype, ht1 in Block-1, showed protective effect to schizophrenia ($p=0.04$).

Conclusion : The results strongly suggest that genetic variations in G72/G30 gene might have significant influence on the pathogenesis of schizophrenia.

References:

1. 1. Chumakov I et al; Genetic and physiological data implicating the new human gene G72 and the gene for D-amino acid oxidase in schizophrenia. PNAS 2002; 99(21) : 13675-13680.
2. 2. Mulle JG et al. No evidence for association to the G72/G30 locus in an independent sample of schizophrenic families Mol Psychiat 2005; 10 : 431-433.

NR609 Tuesday, May 23, 3:00 PM - 5:00 PM

Patterns of Antidepressant Treatment Response in an Employed Population

Eric Wu, Ph.D. *Analysis Group Inc., 111 Huntington Avenue 10th Floor, Boston, MA, 02199,* Howard Birnbaum, Ph.D., Rym Ben-Hamadi, M.S., Jackson Tang, B.S., Paul Greenberg, M.A., Isabelle Gilloteau, M.S., Elisheva Smadja, M.S.

Educational Objectives:

At the conclusion of this presentation, the participant would know how adults diagnosed with major depressive disorder respond to antidepressant treatment and how well they adhere to treatment. A participant would recognize that patients who maintain therapy or those with better medication adherence had lower rates of mental comorbidities, and fewer emergency visits and hospitalizations than patients who switched therapies or were on combination antidepressants therapy.

Summary:

Objective: Describe patterns of patient response to antidepressant treatments, and associated comorbidities, substance abuse, injuries/accidents, emergency visits, and hospitalizations, in an employed population.

Methods: We examined 1999-2003 data from a large U.S. claims database for employees aged 18-64, with at least one diagnosis of MDD (ICD-9: 296.2x, 296.3x) and at least one prescription of selective 5HT or seratonin/norepinephrine reuptake inhibitor (SSRI/SNRI). Patients were classified as switchers, combination antidepressant therapy users (CT), discontinuers, or monotherapy maintainers based on their treatment pattern in the 12-months following SSRI/SNRI initiation. Medication adherence was classified as high, medium, or low using the medication posses-

sion ratio. Annual rates of mental and physical comorbidities, substance abuse, injuries/accidents, as identified using ICD-9 codes, along with emergency visits and hospitalizations were compared across treatment patterns and medication adherence categories.

Results: Of the 3,990 patients, 19.8% were switchers, 18.4% CT, 45.0% discontinuers, and 16.8% maintainers. Switchers and CT had higher rates of mental comorbidities than discontinuers and maintainers (36.8%, 32.5%, 20.6%, and 18.2%, respectively, p<0.001), particularly for anxiety (27.5%, 19.7%, 14.5%, and 13.0%, respectively, p<0.001), higher rates of substance abuse (9.5%, 9.0%, 4.7%, and 2.8%, respectively, p<0.001), and more hospitalizations (p<0.001). Moreover, maintainers had fewer injuries/accidents (30.4% versus 36.9% for switchers; 33.2% for CT; 35.2% for discontinuers, p=0.048) and fewer emergency visits (11.6% versus 16.3% for switchers; 12.0% for CT; 16.6% for discontinuers, p=0.001). Patients with higher medication adherence had lower rates of mental comorbidities, and fewer emergency visits and hospitalizations (all p<=0.023).

Conclusion: Patients who switched therapies or were on combination therapy had higher rates of mental comorbidities, substance abuse and more hospitalizations than patients who maintained therapy. Maintainers and those with higher medication adherence had the lowest rates of mental comorbidities, and fewer emergency visits and hospitalizations.

References:

1. Culpepper L, Rakel RE. The Role of Atypical Antipsychotics in Depression in Primary Care. Companion J Clin Psychiatry 2003;5[suppl 3]:33'37.
2. Mullins CD, Shaya FT, Meng F, et al. Persistence, switching, and discontinuation rates among patients receiving sertraline, paroxetine, and citalopram. Pharmacotherapy. 2005 May;25(5):660-7.

NR610 Tuesday, May 23, 3:00 PM - 5:00 PM

The Effect of 1 Hz Repetitive Magnetic Stimulation on Cell Behavior of PC12

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Educational Objectives:

At the conclusion of this presentation, the participants should be able to recognize the new development in repetitive magnetic stimulation study at cellular level. The participant will be able to know some ongoing edge cutting knowledge about the potential mechanism of how magnetic stimulation may produce global effect in the neurological system. This presentation will also help participant understand why the intensity, longitude and other parameters used in clinical repetitive Transcranial Magnetic Stimulation treatment are important for desirable clinical effect.

Summary:

We are presenting a study of low frequency repetitive magnetic stimulation (rMS) effect on the behaviors of PC12 cell. **Methods**: In a 2X4 design, PC12 cells were divided into two main treatment arms, rMS only and rMS combined with nerve growth factor (NGF). In each arm, there were three rMS treatment intensities plus 0 as the control group: 0.38T, 1.14T, and 1.9T. Total of 10 stimulations at frequency of 1Hz apply to the cells for about 10 seconds each day and the treatment continued for a total of 9 days. The proliferation and neurite extension of PC12 cells was observed via inverse microscopy every day. Dopamine (DA) level in the culture medium was measured on the 3rd, 6th, and 9th day of treatment. **Results**: The 1 Hz rMS significantly facilitated the enation of neurite on PC12 cells at three rMS intensities. The effects size seemed dependent on magnetic intensity: the groups under 1.14T and 1.9T rMS treatment were significantly more likely to grow neurite than the 0.38T group. The extracellular DA levels yielded significant increase in the group under 0.38T stimulation but tended to decrease in the higher intensity groups during the observed period. NGF displays different effects on observed cell behaviors. Overall it facilitated the enation of neurite but decreased the DA level. In combination, rMS plus NGF produced augmentation effect at 0.38T and 1.14T but deduction effect at 1.9T for the enation of neurite and varied on DA level. **Conclusion**: Low-frequency 1 Hz rMS to the PC12 cells might facilitate cell differentiation and change the extracellular DA level. The results suggested that the size or direction of these effects may depend on stimulation intensity. The combination of rMS and NGF may produce different effects depending on the intensity of the stimulation.

References:

1. Keck ME, Welt T, Muller MB, et al. Repetitive transcranial magnetic stimulation increases the release of dopamine in the mesolimbic and mesostriatal system. Neuropharmacology. 2002 Jul;43(1):101-9.
2. Ikeda T, Kurosawa M, Uchikawa C,et al. Modulation of monoamine transporter expression and function by repetitive transcranial magnetic stimulation. Biochemical & Biophysical Research Communications, 2005,327:218-224.

NR611 Tuesday, May 23, 3:00 PM - 5:00 PM

Citalopram May Decrease Smoking in Patients Seeking Treatment for Panic Disorder

Irem Yalug *Kocaeli University Medical Faculty, Gardenya 5/5B Daire:40 Atasehir, Istanbul, Turkey*, Eylem Ozten, Ali Evren Tufan, Sibel Isik

Educational Objectives:

At the conclusion of this presentation the participant should be able to recognise that citalopram may help in treating substance abuse.

Summary:

Object: Panic disorder and smoking are strongly correlated. Daily smoking increases risk for later onset of panic attack and panic disorder. This study is designed to clarify the prevalence of smoking and effect of treatment on smoking status in patients seeking treatment for panic disorder from a university clinic.

Method: Records of 483 patients treated with the diagnosis of panic disorder between 1998-2005 years from the psychiatry clinic of Kocaeli University Medical Faculty were reviewed retrospectively. One way-ANOVA is used to determine the mean number of cigarettes smoked in each treatment group. SPSS 11.0 program is used for statistical analyses and P was set at 0.05.

Results: The prevelance of smoking was 23.6 %. Smoking was significantly less in the groups being treated with citalopram (F= 3.102, P=0.001).

Discussion: Citalopram may decrease substance abuse in patients with panic disorder. Bupropion, clonidine and nortriptyline were also found to be effective it treatment of smoking. Because these also have anxiolytic and antidepressant action, it may be prudent to use these in treatment of panic disorder patients who smoke. Prospective studies are needed to clarify the effect of citalopram on substance abuse.

References:

1. Caldirola D, Bellodi L, Cammino S, Perna G: Smoking and respiratory irregularity in panic disorder. Biol Psychiatry 2004; 56 (6): 393-398.

2. Amering M, Bankier B, Berger P, Griengl H, Windhaber J, Katschnig H: Panic disorder and cigarette smoking behavior. Compr Psychiatry 1999; 40 (1): 35-38.

NR612 Tuesday, May 23, 3:00 PM - 5:00 PM

The Effects of the Switch of Conventional Neuroleptics to Atypical Antipsychotics: A Follow-Up Study of Patients With Chronic Schizophrenia

Norberto M. Zelaschi, Sr., M.D. *Dr. a. Korn Hospital, Psychiatry, 44 No 325 - 4 to B, 520 y 175, Buenos Aires, 1900, Argentina,* Juana L. Rodriguez, Sr., M.D., Sergio Gaitan, Sr., M.D., Maria E. Palacios Vallejos, Sr., Psy.D., Luis M. Zieher, Sr., M.D.

Educational Objectives:

Educational Objectives: The aim of this study is to show the results of the switch of typical antipsychotic treatment (polypharmacy) to a monotherapy treatment with clozapine, risperidone, or olanzapine in schizophrenic patients. As well as, to optimize the rational use of antipsychotic therapy.

Summary:

Introduction: Previous studies suggests that a numerous patients might present lack of response to newer atypical antipsychotics (AAP). We hypothesize a different response to AAP in chronic schizophrenia.

Methods: We studied a group of 39 inpatients with Schizophrenia (DSM IV criteria) with more than 5 years of hospitalization; informed consent was given. Relapses were evaluated in a open naturalistic design. The comparison was done between clozapine (clz),risperidone (ris) and olanzapine (olz). Generic drugs were used. The complete follow-up period was 24 months. The evaluations were monthly the first 6 months, and later every 3 months. Chi square test was used to analyze the results of treatment. All the figures are expressed in average +/- 1SD.

Results: The average age was 48.20 (8.28). Drugs : CLZ: n= 12, d/d=200-400 mg..RIS : n=14, d/d= 2-6 mg.: OLZ n=13,d/d= 20-60mg :

The incidence of relapse rate was. after first year of treatment : CLZ (n=0), RIS (n=5), OLZ (n=10), :x2 = 17.02 : p=0.000, and during the second year :CLZ (n=0), RIS (n=11), OLZ, (n=11): x2 = 29.17 : p=0.000

Conclusions: We suggest a better outcome of the CLZ compared to the RIS and OLZ, particularly considering long-term treatment: The data found could be explained by patients with treatment resistence, along with prolonged hospitalization.

References:

1. Journal Article-Lieberman JA, Stroup TS, McEvoy JP, Swartz MS,et.al Effectiveness of Antipsychotic Drugs in Patients with Chronic Schizophrenia Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) Investigators. N Engl J Med. 2005 Sep.

2. Journal Article- Davis JM, Chen N, Glick ID: A meta-analysis of the efficacy of second-generation antipsychotics., Arch Gen Psychiatry. 2003 Jun;60(6):553-64.

NR613 Tuesday, May 23, 3:00 PM - 5:00 PM

The Impact of Combined Treatment in Schizophrenic Patients

Norberto M. Zelaschi, Sr., M.D. *Dr. A.Korn Neuropsychiatric Hospital, 44 No 325 - 4 to B, La Plata ,Buenos Aires, Argentina, 1900, Argentina*, Maria E. Palacios Vallejos, Sr., Psy.D., Juana L. L. Rodriguez, Sr., M.D., Sergio Gaitan, Sr., M.D., Luis M. Zieher, Sr., M.D.

Educational Objectives:

The objective of this study is to show the importance of a combined treatment in schizophrenic patients, taking into account other therapies which could make a difference in the social outcome.

Summary:

Introduction: Schizophrenic disorders are complex. The treatment is based on drugs, psychotherapeutic and psychosocial rehabilitation.

Method We have studied 20 patients with the diagnosis of schizophrenia (DSM IV criteria) treated with therapeutic doses with conventional antipsychotics haloperidol (n=10),and with atypical antipsychotics clozapine (AAP) (n=10). Ten patients received a combined treatment with psychosocial and cognitive rehabilitacion.

The following characteristics were evaluated the neurocognitive functioning (working memory and executive functions), psychopathology (positive and negative symptoms according to the PANSS scale) and Quality of Life Scale(QLS).

Anova test (Kruskall-Wallis) was used to detect differences between the groups, and the Wilcoxon test was utilized to evaluate if the results of the treatment produced changes.

Results:No significant differences were found in the ages of patients studied (p=0.49).

The first evaluation of stage 1 of the combined treatment there was no significant difference of the groups studied, except in the (QLS).

The PANSS expresses that no significant difference of the negative symptoms were found, but if we compare the result before and after the combined treatment, group 1 with typical antipsychotics (TAP), the symptoms descended significantly after the treatment.This reduction is important because of the impact of the social outcome of the patients.

The(QLS) showed that the differences found between the groups (Anova Kruskall-Wallis p=0.01) groups 1 TAP, II AAP and IV AAP differ significantly from Group III TAP, and also the difference between the groups (Wilcoxon Group I TAP p=0.01).

Conclusions:Patients who recieved a combined program of treatment (medication + psychosocial and cognitive rehabilitation) had a better quality of life independently of the medication they have recieved. As long as that the combined treatment develops and strengths the individual resources to deal with stress, and there exists a social network to reduce enviromental and personal stressors that could prevent relapse.

References:

1. Book-Foster Green M.:". Schizophrenia from a Neurocognitive Perspective. Proving the impenetrable darkness". Ed. Allyn and Bacon 1998.

2. Harvey P, Keefe R. Studies of cognitive change in patients with schizophrenia following novel antipsychotic treatment. American Journal of Psychiatry 2001; 158 (2) :176-184.

NR614 Tuesday, May 23, 3:00 PM - 5:00 PM

Adherence Levels and Differential Use of Mental Health Services in the Treatment of Schizophrenia

Nicolas M. Furiak, M.S. *Indianapolis, IN*, Baojin Zhu, Haya Ascher-Svanum, Douglas E. Faries, William Montgomery

Educational Objectives:

At the conclusion of this presentation, the participant should recognize that in the treatment of schizophrenia in usual care, a differential use of psychiatric services is associated with a patients' level of adherence with antipsychotic medications. Adherence with antipsychotic medication regimens appears to be associated with

lower risk of hospitalization and emergency room visits, and greater engagement in the outpatient treatment process.

Summary:

Objectives: To compare annual mental health service utilization patterns by level of adherence with antipsychotic medication in the naturalistic treatment of schizophrenia.

Method: Data were drawn from a large prospective naturalistic study of treatment for patients with schizophrenia in the U.S, conducted between 7/1997 and 9/2003. Detailed mental health resource utilization was systematically abstracted from medical records and augmented with patients' self report. Annual medication possession ratio (MPR) with any antipsychotic was calculated, and each participant was categorized into 1 of 3 adherence groups: adherent (MPR>=80%, N=1758), partially adherent (60%≤MPR<80%, N=36), and non-adherent (MPR<60%, N=216).

Results: Adherent participants were least likely to have any psychiatric hospitalization and emergency room visits ($p<0.05$). Compared to non-adherent, adherent participants were also significantly more likely to be engaged in outpatient treatment processes as evident by greater likelihood of participation in any psychosocial group intervention ($p<0.05$) and in any medication management with psychiatrists ($p<0.05$). **Conclusions:** Medication adherence levels are associated with differential use of psychiatric services. Adherence appears to be associated with lower risk of hospitalization and emergency room visits and greater engagement in the outpatient treatment processes.

References:

1. Gilmer TP, Dolder CR, Lacro JP, Folsom DP, Lindamer L, Garcia P, Jeste DV: Adherence to treatment with antipsychotic medication and health care costs among Medicaid beneficiaries with schizophrenia. Am J Psychiatry 2004; 161:692-699.
2. Ascher-Svanum H, Faries D, Zhu B, Ernst F, Swartz M, Swanson J. Medication Adherence and Long-Term Functional Outcomes in the Treatment of Schizophrenia in Usual Care. J Clin Psychiatry, in press.

NR615 Tuesday, May 23, 3:00 PM - 5:00 PM

Predictors of Diabetes in an Observational Study of Olanzapine Versus Divalproex in the Treatment of Bipolar Disorder

Baojin Zhu *Eli Lilly and Company, Lilly Research Laboratories, Indianapolis, IN, 46285*, Haya Ascher-Svanum, Douglas E. Faries, John P. Houston, Ilya Lipkovich, Michael Stensland, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should recognize that risk factors for new onset diabetes among bipolar patients are similar to those found in the general population.

Summary:

Objective: To assess the risk factors associated with diabetes among patients with bipolar disorders treated in usual care.

Methods: Data were obtained from a 1-year, non-randomized observational study comparing olanzapine and divalproex in the treatment of bipolar disorder.

Patients with new onset diabetes were diagnosed or treated with anti-diabetic agents during the study, others reported having diabetes at enrollment. Pre-existing risk factors for diabetes, weight change, development of hyperlipidemia, and medication type were studied. Stepwise Cox proportional hazards models were used to identify the best predictors of developing new onset diabetes.

Results: The 1-year prevalence of diabetes was 8.8% (32/363) (olanzapine N=16, divalproex N=16), including 2.7% new onset diabetes (10/363) (olanzapine N=6, divalproex N=4). BMI at baseline, non-Caucasian ethnicity, age>=40, pre-existing depression, heart conditions and metabolic conditions, family history of diabetes, and asthma were associated with higher likelihood of having diabetes. Hyperlipidemia, history of hypertension, and family history of asthma were significant predictors of new onset diabetes.

Conclusion: Risk factors for diabetes among bipolar patients are similar to those found in the general population. Risk factors for pre-existing diabetes appear congruent with risk factors for new onset diabetes, whereas medications appear not to be significant predictors of new onset diabetes.

References:

1. Morriss R, Mohammed FA. Metabolism, lifestyle and bipolar affective disorder. J Psychopharmacol. 2005;19(6 Suppl):94-101.
2. Cavazzoni P, Mukhopadhyay N, Carlson C, Breier A, Buse J. Retrospective analysis of risk factors in patients with treatment-emergent diabetes during clinical trials of antipsychotic medications. Br J Psychiatry Suppl. 2004;47:S94-101.

NR616 Wednesday, May 24, 12:00 PM - 2:00 PM

Escitalopram Treatment of Kleptomania: A Double-Blind Discontinuation Trial

Elias Aboujaoude *Stanford University, Psychiatry and Behavioral Sciences, 401 Quarry Road, Ste 2301A, Stanford, CA, 94305-5546*, Lorrin M. Koran, Nona Gamel

Educational Objectives:

Upon attending a presentation of this poster, the attendee will be familiar with the basics in diagnosing and treating kleptomania, and will be aware of the results of the first double blind placebo controlled trial testing a medication in the treatment of this condition.

Summary:

Background: Kleptomania involves stealing unneeded items or items of limited value from shops, strangers and acquaintances. Cases of successful treatment are reported with SSRIs, naltrexone and cognitive behavioral therapies. We conducted the first double-blind, placebo-controlled trial of pharmacotherapy for kleptomania, using the SSRI escitalopram. Methods: We enrolled adults aged at least 20 with DSM-IV-defined kleptomania of > 1 year's duration, and marked by court referral or stealing > once/week. Subjects received open-label escitalopram 10 mg/day for 4 weeks and if not "much improved," took 20 mg/day for 3 additional weeks. "Response" was defined as > 50% decrease in thefts/week and a Clinical Global Impressions-Improvement score of much or very much improved. Responders at week 7 were randomized to 16 weeks of double-blind escitalopram at the week 7 dose or to placebo. Results: We enrolled 24 subjects, with a mean age of 49.5 years.Open-label phase: The mean (± SD) score on the Yale-Brown Obsessive-Compulsive Scale-Kleptomania Version (YBOCS-KV) decreased from 21.5 (± 4.9) at baseline to 7.3 (± 6.9) at the end of week 7. Mean thefts/week decreased from 4.0 ± 3.3 (range 1 - 17) to 0.9 (± 1.2) (range 1-4). Week 7 percent changes from baseline in YBOCS-SV and Montgomery Asberg Depression Rating Scale (MADRS) scores were not significantly correlated. Nineteen subjects (79%) were responders and 15 were randomized. Five subjects withdrew early (four responders). Double-blind phase: Three of seven (43%) subjects assigned to escitalopram relapsed compared to 4/8 (50%) assigned to placebo (Fisher's Exact test p = .38). Probability of relapse was unrelated to kleptomania severity, as measured by Y-BOCS-SV score, at baseline or at randomization. Conclusion: A placebo response underlying the open-label findings is the most likely explanation of appar-

ently favorable open-label results. A true drug effect in some subjects, cannot, however, be ruled out.

References:

1. Koran, LM: Obsessive Compulsive and Related Disorders in Adults. Cambridge, Cambridge University Press, 1999.
2. Aboujaoude E: Overview of kleptomania and phenomenological description of forty patients. Prim Care Companion J Clin Psychiatry 2004; 6(6):244-247.

NR617 Wednesday, May 24, 12:00 PM - 2:00 PM

Escitalopram for Compulsive Shopping Disorder: A Double-Blind Study

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Educational Objectives:

At the conclusion of this presentation, attendees will have an appreciation for compulsive shopping disorder: its presentation, epidemiology and treatment approaches. They will also be aware of the results of a double blind medication trial testing escitalopram in the treatment of this condition.

Summary:

Background: A double-blind discontinuation trial suggested that citalopram is effective in treating compulsive shopping disorder. We conducted an identically designed trial, with 7-weeks of open-label escitalopram treatment followed by a 9-week double-blind, placebo-controlled discontinuation period to test whether escitalopram is effective.

Methods. We recruited adult outpatients meeting suggested diagnostic criteria and having a score of ≥ 17 on the Yale-Brown Obsessive-Compulsive Scale-Shopping Version (YBOCS-SV). Open-label escitalopram was started at 10 mg/day and increased after four weeks, absent marked response and limiting side effects, to 20 mg/day. Responders at week 7 were randomized to 9 weeks of double-blind escitalopram at their week 7 dose or to placebo.

Results. We enrolled 26 women. Mean (± SD) Y-BOCS-SV scores decreased significantly from 24.5 (±3.9) at baseline to 9.9 (± 9.3) at week 7 (mean decrease = 57.5%, t = -7.18, p <.001). Nineteen of 26 subjects (73%) met responder criteria, but one refused randomization and one was withdrawn for protocol violation before the first double-blind evaluation. Of the 17 responders in the double-blind treatment phase, 63% (5/8) randomized to escitalopram relapsed (Y-BOCS-SV ≥ 17 and "minimally improved" or less on the Clinical Global Impressions-Improvement scale) compared with 67% (6/9) randomized to placebo (Fisher's Exact Test p = .38).

Conclusions. Escitalopram may not be generally effective for Compulsive Shopping Disorder, or the therapeutic effect may be lost for many individuals after a few months at constant dose. Larger, double-blind studies using a parallel groups design are needed to evaluate the role of SSRIs in the treatment of Compulsive Shopping Disorder.

References:

1. Koran LM. Obsessive-Compulsive and Related Disorders in Adults: A Comprehensive Clinical Guide, New York: Cambridge University Press, 1999.
2. Black DW. Compulsive shopping disorder: definition, assessment, epidemiology and clinical management. CNS Drugs 2001;15:17-27.

NR618 Wednesday, May 24, 12:00 PM - 2:00 PM

Response to Extended-Release Dexmethylphenidate in Adults With Moderate or Severe ADHD

Lenard A. Adler, M.D. *New York University School of Medicine, Psychiatry, 530 First Avenue HCC 5A, New York, NY, 10016-6497*, Thomas J. Spencer, M.D., Linda Pestreich, B.S.C., Jim Wang, Ph.D., Rafael Muniz, M.D.

Educational Objectives:

At the end of this presentation, the attendee should be able to:
Describe the scope and time course of response to d-MPH-ER in adults with ADHD.
Recognize how treatment responses may differ according to baseline illness severity.

Summary:

Objectives: The efficacy and safety of extended-release dexmethylphenidate (d-MPH-ER) were demonstrated in a multicenter, double-blind, placebo-controlled trial of 221 adults with ADHD. This post-hoc analysis compared d-MPH-ER's efficacy in patients with moderate versus severe illness at baseline.

Method: Patients (18-60 years old) with DSM-IV-defined ADHD were randomized to once-daily d-MPH-ER doses of 20 mg (n= 58), 30 mg (n=55), 40 mg (n=55), or placebo (n=53) for 5 weeks. The primary efficacy variable was change from baseline in DSM-IV ADHD-RS total score. Secondary efficacy variables included change from baseline in ADHD-RS Inattentiveness and Hyperactivity/Impulsivity subscales. Baseline Clinical Global Impressions-Severity (CGI-S) scores of 3 or 4 were defined as moderate illness, and baseline scores of 5 or 6 were defined as severe illness.

Results: For all patients, mean change from baseline in ADHD-RS total score was 7.9 for placebo, 13.7 for d-MPH-ER 20 mg (P=.006), 13.4 for d-MPH-ER 30 mg (P=.012), and 16.9 (P<.001) for d-MPH-ER 40 mg. For those with moderate illness, respective improvements were 8.64, 14.86, 11.77, and 14.94. For those with severe illness, respective improvements were 6.60, 11.62, 14.93, and 19.77. Similar results were observed in Inattentiveness and Hyperactivity/Impulsivity scores. Trends toward dose-response relationships were clearer in those with severe versus moderate illness. Regardless of baseline severity, all dosage groups showed increasing changes from baseline to week 5.

Conclusions: The effectiveness of d-MPH-ER 20-40 mg extends to patients with moderate or severe ADHD. Relationships between dose and efficacy may be more pronounced in patients with severe illness, suggesting that dose titration strategies may need to be tailored based on initial severity. For both moderate and severe illness, symptomatic improvement appears to increase over the first several weeks of treatment.

Supported by funding from Novartis Pharmaceuticals Corporation.

References:

1. Keating GM, Figgitt DP: Dexmethylphenidate. Drugs 2002; 62:1899-1904.
2. Spencer T, Kim S, Jiang H, et al: Efficacy of dexmethylphenidate extended-release capsules in adults with attention-deficit/hyperactivity disorder. Presented at: 157th Annual Meeting of the American Psychiatric Association; May 1-6, 2004; New York,NY.

NR619 Wednesday, May 24, 12:00 PM - 2:00 PM

Chart Review of Patients Receiving Immediate Release d-Methylphenidate Augmentation of Sustained Release Stimulants

Lenard A. Adler, M.D. *New York University School of Medicine, Psychiatry, 530 First Avenue HCC 5A, New York, NY, 10016-6497*, Melinda S. Morrill, C.S.W., Lisa Reingold, B.A.

Educational Objectives:

1. Participants will better understand d-Methylphenidate augmentation of sustained release stimulants.
2. Participants will better understand factors that may influence duration and tolerability of d-Methylphenidate as a supplement to long-acting stimulants.

Summary:

Objective: To investigate d-methylphenidate as a supplemental treatment to long-acting stimulants for ADHD.

Methods: As part of an ongoing IRB approved chart review, we examined ADHD patients (N=27) treated clinically in the NYU School of Medicine Department of Neurology ADHD program between 1/31/02-7/26/04 who received d-methylphenidate to augment mixed-amphetamine salts XR, OROS methylphenidate, or methylphenidate Extended Release . The diagnosis of ADHD had been established by a structured clinical interview (K-SADS ADHD module for children and adolescents and ACDS v1.2 for adults). 74% (20) of patients were adults, 45% (13) were male and their ages ranged from 8 to 51 years old (mean = 29.7 + 13.4 SD years). 19 received d-methylphenidate in the afternoon and 8 received d-methylphenidate in the afternoon and in the morning. 9 patients received concomitant treatment with atomoxetine. d-methylphenidate treatment characteristics (dose and length of treatment) and clinical efficacy ascertained by patient report were examined. Possible factors influencing dosing of d-methylphenidate were also examined.

Results: Daily d-methylphenidate treatment ranged from 2.5-30 mg (mean = 6.94 mg/day + 6.7 SD). The mean clinical reported duration of effect of afternoon d-methylphenidate was 4.94 hours +0.5 SD (range: 3-6 hours). The prescribed dose of d-methylphenidate correlated with the total daily dose of sustained-release stimulant therapy. 26 patients reported clinical improvement. d-methylphenidate was well tolerated; only two patients reported dose-limiting side-effects (agitation, early insomnia).

Conclusions: d-methylphenidate was successful in extending the duration of effect for ADHD patients receiving treatment with sustained-release stimulants.

Supported by an unrestricted educational grant from Novartis Pharmaceuticals Corporation.

References:

1. Adler LA, Chua H: Management of ADHD in Adults. Journal of Clinical Psychiatry 2002; 63 Suppl 12:29-35.
2. Adler LA: Adult ADHD, Institute on Adult Presentation of Childhood Disorders, American Academy of Child and Adolescent Psychiatry, Washington D.C., October, 2004.

NR620 Wednesday, May 24, 12:00 PM - 2:00 PM

Chart Review of Atomoxetine Treated ADHD Patients With and Without Stimulants

Lenard A. Adler, M.D. *New York University School of Medicine, Psychiatry, HCC 5A, 530 First Avenue, New York, NY, 10016-6497*, David M. Shaw, B.A., Franny Raphael, B.S.

Educational Objectives:

1. Participants will better understand the efficacy of combination atomoxetine and stimulant therapy.
2. Participants will better understand factors that may influence tolerability of combination atomoxetine and stimulant therapy.

Summary:

Objective: To compare the clinical effects and tolerability of standard clinical treatment with atomoxetine in combination with stimulant treatment in patients with ADHD. **Methods:** As part of an ongoing, retrospective, IRB-approved chart review, we examined consecutive ADHD patients (n= 29) treated over 7 months with atomoxetine therapy at the NYU Departments of Psychiatry and Neurology ADHD Program. ADHD diagnoses were established by a semi-structured interview (ADHD Module from K-SADS for children and adolescents and ACDS v1.2 for adults) and a DSM-IV clinical interview for co-morbidities. Age ranged from 6 to 60 (mean 38.3 ±12.1 years). 68.9% (20) were male. We compared the effect of combination treatment course on the following parameters: (1) clinical success and tolerability of therapy (2) the impact of co-morbidity on efficacy and tolerability and (3) possible effects of dosing. **Results:** Treatment was well tolerated, with 75.9% (22) of the patients reporting acceptable tolerability. All of the patients who tolerated the therapy elected to receive ongoing treatment with atomoxetine and stimulants. Co-morbidities were not found to significantly inhibit tolerability or efficacy. Average starting atomoxetine dose was 17.2 ± 4.3 mg/day, which reflected the fact that atomoxetine was being used as an augmentation strategy. Tolerability did not seem to be affected by the stimulant dose (average final stimulant 41.4 +/- 33.6 mg/day in methylphenidate equivalents). **Conclusions:** These preliminary results indicate that atomoxetine can be safely and effectively combined with stimulants to treat adolescent and adult ADHD and may be suitable for patients who have shown inadequate responses to either therapy on its own. This research is partially supported by an unrestricted grant from Eli Lilly and Company.

References:

1. Brown TE: Atomoxetine and Stimulants in Combination for Treatment of Attention Deficit Hyperactivity Disorder: Four Case Reports. J Child Adolesc Psychopharmacol 2004; 14(1):129-136.
2. Kratochvil CJ, et al. Atomoxetine and methylphenidate treatment in children with ADHD: a prospective, randomized, open-label trial. J Am Acad Child Adolesc Psychiatry. 2002 Jul; 41(7):776-84.

NR621 Wednesday, May 24, 12:00 PM - 2:00 PM

Issues in the Treatment and Diagnosis of ADHD by Primary Care Physicians

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Educational Objectives:

1. To recognize a relative lack of understanding regarding adult Attention Deficit-Hyperactivity Disorder (ADHD) by primary care physicians.
2. To understand differing rates of referral and treatment of adults with ADHD by PCPs.

Summary:

Objective: To investigate the experiences and attitudes of primary care physicians (PCPs) in the diagnosis and treatment of ADHD in adults using a on-line survey. Methods: 400 primary care physicians who commonly treated mental health disorders were surveyed in this IRB approved study as to their views regarding ADHD versus other mental health disorders, such as depression and GAD. Results: The survey illustrated that PCPs considered themselves more knowledgeable about depression and GAD than they do about ADHD, and that PCPs were uncomfortable diagnosing adult ADHD. Approximately half (48%) were unconfident diagnosing adult ADHD and thought that the diagnostic criteria for adult ADHD are unclear (44%). Three-quarters of PCPs rated the quality and accuracy of diagnostic tools available for adult ADHD as poor or fair. The majority of PCPs believed that (1) adult ADHD is not well understood by the medical community (77%), (2) it is more difficult to diagnose adults with ADHD than it is to diagnose children (72%), and (3) the underlying ADHD symptoms are similar

in children and adults, but the manifestations of these symptoms differ throughout the life course (73%). Additionally, PCPs were much more likely (65%) to defer to a specialist when diagnosing adult ADHD than for depression (2%) or GAD (3%). Conclusion: This survey underlines a need for increased education and teaching about ADHD in the primary care community. This research was funded by an unrestricted educational grant from Eli Lilly and Company.

References:

1. Elliot H. Attention deficit hyperactivity disorder in adults: a guide for the primary care physician. South Med J. 2002; 95(7):736-742.
2. Spencer T, Biederman J, Wilens T, Faraone SV. Is attention-deficit hyperactivity disorder in adults a valid disorder? Harv Rev Psychiatry. 1994 Mar-Apr; 1(6):326-335.

NR622 Wednesday, May 24, 12:00 PM - 2:00 PM

Duloxetine as an Effective Treatment for Improving Painful Physical Symptoms and Functioning Associated With GAD

Christer Allgulander, M.D. *Karolinska Institute, M57 Huddinge Hospital, Huddinge, 141 86, Sweden*, Hannu J. Koponen, M.D., Janelle Erickson, Ph.D., Yili Pritchett, Ph.D., Michael J. Detke, M.D., Susan G. Ball, Ph.D., James M. Russell, M.D.

Educational Objectives:

At the end of this presentation, participants will be knowledgeable that duloxetine is an effective treatment for improving painful physical symptoms and functional outcomes in patients with generalized anxiety disorder.

Summary:

Objective: Painful physical symptoms are increasingly recognized as a significant morbidity associated with anxiety disorders.[1] This study examined the efficacy and safety of duloxetine, a balanced and potent dual reuptake-inhibitor of 5HT and norepinephrine,[2] for treatment of painful physical symptoms and functioning in GAD. *Methods*: In a 9-week, double-blind, fixed-dose study, 507 patients [Mean age=43.78 yrs; 67.8% female] with a DSM-IV defined GAD diagnosis were randomly assigned to receive duloxetine 60 mg/day (DLX-60mg, N=168), duloxetine 120 mg/day (DLX-120mg, N=170), or placebo (PBO, N=175). Pain was assessed using Visual Analogue Scales for Pain. Other measures of patient functioning included the Sheehan Disability Scale (SDS), the Quality of Life Enjoyment and Satisfaction Questionnaire-Short Form (Q-LES-Q-SF) and EuroQoL-5D. Changes from baseline to endpoint in measures were analyzed using ANCOVA. *Results:* Compared with PBO, both DLX groups demonstrated significantly greater reduction in ratings for each pain item: overall pain ($P<.02$), headaches ($P<.05$), back pain ($P<.001$), shoulder pain ($P<.01$), interference due to pain ($P<.02$), and pain during waking hours ($P<.001$). The DLX groups also demonstrated greater improvement, compared with PBO group, in all domains of the SDS ($P<.001$), in the Q-LES-Q-SF total score ($P<.001$) and EuroQol index ($P<.01$) and health state scores ($P<.001$) No significant differences were found between the two DLX groups. *Conclusions*: Within patients with GAD, who were not selected for the occurrence of pain, treatment with duloxetine 60mg and 120mg once daily resulted in significant improvement in painful physical symptoms. Duloxetine also enhanced patients' quality of life and overall functioning.

References:

1. McWilliams LA, Goodwin RD, Cox BJ. Depression and anxiety associated with three pain conditions: Results from a nationally representative sample. Pain 2004: 111: 77-83.
2. Bymaster FP, Dreshfield-Ahmad LJ, Threlkeld PG, Shaw JL, Thompson L, Nelson DL,. Hemrick-Luecke SK, Wong DT: Comparative affinity of duloxetine and venlafaxine for serotonin and norepinephrine transporters in vitro and in vivo, human serotonin recept.

NR623 Wednesday, May 24, 12:00 PM - 2:00 PM

Abrupt Conversion From Oral Methylphenidate to a Transdermal Patch

L Eugene Arnold, M.D. *Ohio State University, Nisonger Center, 1581 Dodd Drive, Columbus, OH, 43210*, Anil Patel, M.D., Thomas Rugino, M.D., Louise Beckett, M.D., Michael J. McKay

Educational Objectives:

At the conclusion of this presentation, the participant should be able to: Describe the clinical use of the methylphenidate transdermal system (MTS) in pediatric subjects who were previously treated with oral extended-release methylphenidate. Discuss ratings of efficacy and safety in a naturalistic setting.

Summary:

Objective: To evaluate the efficacy and safety of methylphenidate transdermal system (MTS) in children with ADHD previously treated with oral extended-release methylphenidate and abruptly converted to an equivalent-dose MTS.

Method: This was a multi-center, open-label conversion study of MTS in children aged 6-12 years with DSM-IV ADHD successfully treated with Ritalin LA, Concerta, or Metadate CD. Subjects were abruptly converted from oral extended-release methylphenidate to an equivalent-dose MTS using a predefined dose-transition schedule. Efficacy was primarily assessed by change in ADHD Rating Scale-IV (ADHD-RS-IV) scores, secondarily by Clinical Global Impression (CGI).

Results: 82 subjects are included in this interim analysis. At study endpoint, on the ADHD-RS-IV (range 0-54 with lower score better), the change from Ritalin LA was +1.9 ($p=0.60$), from Metadate CD -3.0 ($p=0.11$) and from Concerta -2.1 ($p=0.04$). On the CGI-Improvement Scale, 29.3% were rated very much improved, 22% much improved, 19.5% minimally improved, 20.7% unchanged, 4.9% minimally worse, 3.7% much worse, and 0% very much worse at study endpoint.

Conclusion: Abrupt conversion from oral extended-release methylphenidate to MTS resulted in improvement or no significant change in clinician-rated efficacy for over 91% of subjects converted. Thus the conversion schedule used in the study appears useful. MTS was generally well-tolerated, with one serious side effect. MTS may be an effective non-oral ADHD treatment.

Supported by funding from Shire US Inc.

References:

1. Wigal S, McGough JJ, Abikoff H, Turnbow J, Posner K, Moon E. Behavioral effects of methylphenidate transdermal system in children with ADHD. Poster presented at the joint meeting of AACAP and CACAP. Toronto, Ontario. October 21, 2005.
2. Findling RL, Lopez FA. The effects of transdermal methylphenidate with reference to OROS methylphenidate in ADHD. Poster presented at the joint meeting of the AACAP and CACAP. Toronto, Ontario. October 20, 2005.

NR624 Wednesday, May 24, 12:00 PM - 2:00 PM

Discontinuation Symptoms in Social Anxiety Disorder, GAD, and Major Depressive Disorder

David S. Baldwin, Dr. Med. Sc. *Community Clinical Sciences, School of Medicine, University of Southampton, Biomedical Sciences Bld, Bassett Crescent East, Southampton, SO16*

7PX, United Kingdom, Stuart A. Montgomery, M.D., Rico Nil, D.Sc., Malcolm Lader, M.D.

Educational Objectives:

The participant will know whether antidepressants differ with respect to discontinuation symptoms, if these symptoms vary between depression and anxiety disorders, and whether the length of treatment affects symptoms.

Summary:

Objectives: This analysis addresses the question whether antidepressants differ with respect to discontinuation symptoms, if these symptoms vary between depression and anxiety disorders, and whether the length of treatment affects symptoms.

Methods: Data came from two comparative studies of escitalopram in MDD (one *versus* venlafaxine XR and one *versus* paroxetine), two studies of escitalopram in long-term treatment of social anxiety disorder (one of which used paroxetine as an active reference), and one study of escitalopram in generalised anxiety disorder, using paroxetine as an active reference. All studies included a defined discontinuation period of 1-2 weeks and used the Discontinuation Emergent Signs and Symptoms (DESS) checklist (1,2) to record the number of discontinuation symptoms. The analysis included 1750 male and female patients treated with escitalopram (n=1051), paroxetine (n=336), venlafaxine XR (n=124) or placebo (n=239).

Results: In all studies and treatment groups, discontinuation symptoms were transient. Based on the increase in total DESS scores, paroxetine and venlafaxine XR showed significantly more discontinuation symptoms than escitalopram (DESS increase= 1.20 for escitalopram *versus* 3.72 for venlafaxine XR; DESS increase =1.62 for escitalopram *versus* 3.34 for paroxetine) in MDD; a significantly lower number of discontinuation-emergent symptoms for escitalopram than for paroxetine was also seen in social anxiety disorder (DESS increase =1.39 for escitalopram *versus* 3.34 for paroxetine) and generalised anxiety disorder (DESS increase =1.20 for escitalopram *versus* 3.78 for paroxetine). No differences in discontinuation symptoms were observed between the three conditions. There was no evidence for increased symptom incidence with longer treatment duration.

Conclusion: These data show that discontinuation profiles differ between antidepressants of the same class (SSRIs) and that these profiles are broadly similar across different diagnoses. No evidence was seen for a higher discontinuation burden with longer treatment.

References:

1. Rosenbaum JF, Fava M, Hoog SL, Ascroft RC, Krebs WB (1998). Selective serotonin reuptake inhibitor discontinuation syndrome: A randomized clinical trial. Biological Psychiatry 44, 77-87.

2. Hindmarch I, Kimber S, Cockle SM (2000). Abrupt and brief discontinuation of antidepressant treatment: effects on cognitive function and psychomotor performance. International Clinical Psychopharmacology 15, 305-318.

NR625 Wednesday, May 24, 12:00 PM - 2:00 PM

Qualitative Changes in Symptomatology With Treatment in GAD and Major Depression

David S. Baldwin, Dr. Med. Sc. *Community Clinical Sciences, School of Medicine, University of Southampton, Biomedical Sciences Bld, Bassett Crescent East, Southampton, SO16 7PX, United Kingdom*, Emmanuelle Weiller, H. Andersen, Y. Lecrubier

Educational Objectives:

The participant will gain understanding of the profile of individual items of anxiety and depression rating scales in patients with pure MDD, pure GAD, and MDD with comorbid anxiety.

Summary:

Objectives: The aim was to investigate the symptom profile as measured by HAMA (1), MADRS (2), and HAD, in patients with either GAD or MDD, or both, before and after treatment, in order to answer two questions: Are these symptomatic profiles initially different? Do the symptomatic profiles change with treatment?

Methods: Data were analysed from all randomised double-blind clinical studies with escitalopram that measured symptoms using HAMA, or MADRS, or HAD: 6 in GAD (n=2008), 13 in MDD (n= 2481) and 1 open study in MDD with comorbid anxiety (n=774). In order to assess the profile independently of severity, the contribution of each item of the HAMA, MADRS, and HAD scales to the total score at baseline and after treatment with escitalopram was evaluated.

Results: Most HAMA symptoms contribute similarly to the total baseline score in GAD patients. In MDD patients, depressed mood and psychic anxiety (anxious mood, tension, insomnia, and concentration) account for most of the HAMA total score. Three symptoms contribute to two-thirds of the MADRS total score in GAD patients (tension, sleep, and concentration), whereas almost all MADRS items contribute equally to the total score in MDD. The symptom profile in GAD and MDD patients using the HAD is consistent with those based on HAMA and MADRS. After treatment with escitalopram, the overall severity of anxiety and depressive symptoms significantly decreased in GAD and MDD patients. No qualitative change was observed after treatment and the symptomatic profiles remain stable in both conditions.

Conclusion: In MDD, anxiety symptoms are common and qualitatively similar to those of GAD whereas 'core' depressive symptoms are uncommon in GAD patients. After treatment with escitalopram, the symptomatic profile is remarkably stable in patients with GAD or MDD, indicating that treatment is probably affecting a common dimension.

References:

1. Hamilton M. (1959) The assessment of anxiety states by rating. British Journal of Medical Psychology 32: 50'55.

2. Montgomery, SA, Åsberg, M. (1979) A new depression scale designed to be sensitive to change. British Journal of Psychiatry 134: 382-389.

NR626 Wednesday, May 24, 12:00 PM - 2:00 PM

Comparison of the Standard Scales and CGI Scores in Major Depressive Disorder, Panic Disorder, Social Anxiety Disorder, and GAD

Borwin Bandelow, Prof. Dr. *University of Goettingen, Von-Siebold-Str 5, Goettingen, D-37075, Germany*, David S Baldwin, M.D., Ornah C. Dolberg, Ph.D., Henning F. Andersen, M.S.C., Dan J. Stein, M.D.

Educational Objectives:

The participant will gain knowledge concerning the relationship between the CGI scale and those specific for anxiety disorders and major depression.

Summary:

Introduction: The Clinical Global Impression [CGI] (1) is commonly used as a global measure for disease severity and treatment-induced improvement in a variety of disorders. The objectives of the present study were to compare the CGI measures with disorder-specific scales that are considered to represent 'gold standard' measures in these disorders, and to define levels for

response and remission for these standard scales, by reference to CGI definitions.

Methods: In a *post-hoc* analysis, randomized controlled studies with patients treated with escitalopram for MDD (n=5), panic disorder (n=1), GAD (n=4), or social anxiety disorder (n=2) were compared with regard to the standardized effect sizes in the Clinical Global Impression (CGI) score and the rating scales that represent the 'gold standard' for these disorders (MADRS, PAS, HAM-A, and LSAS).

Results: In all indications, treatment with escitalopram showed high standardized effect sizes (2) on all efficacy measures. Standardized effect sizes of active drug-placebo differences were numerically higher in panic disorder than in the other disorders but this difference was not significantly different. Moderate to high correlations were found between CGI and the standard scales. The CGI was shown to be a consistent measure of disease severity and to be sensitive to change. When defining "response" to a treatment on a standard rating scale, a ≥50% decease from baseline scale score is conventionally used. However, in this analysis the CGI-I definition of at least 'much improved' corresponded to only 39%, 23%, 42%, and 31% reductions in the MADRS, PAS, HAMA and LSAS, respectively.

Conclusion: The comparison of the standard scales and CGI scores suggest that the traditional definition of response may be too conservative.

References:

1. Guy W (1976): Clinical Global Impression Scale (CGI). ECDEU Assessment Manual for Psychopharmacology. Washington, D.C.: National Institute of Mental Health-US Dept of Health, Education, and Welfare publication (ADM), pp 76-338.
2. Cohen J (1988): Statistical power analysis for the behavioral sciences. New York: Erlbaum.

NR627 Wednesday, May 24, 12:00 PM - 2:00 PM

Atomoxetine for the Treatment of ADHD and Oppositional Defiant Disorder

Mark E. Bangs, M.D. *Lilly Research Laboratories, Lilly Corporate Center, Indianapolis, IN, 46285*, Philip Hazell, M.D., Marina Danckaerts, M.D., David W. Williams, M.S., Rodney J. Moore, Ph.D., Louise R. Levine, M.D.

Educational Objectives:

At the conclusion of this presentation, the attendee should be aware that, in patients with ODD comorbid with ADHD, there are significant improvements in ODD symptoms during treatment with atomoxetine and also the limitations of these data.

Summary:

Objective: This study examined the effectiveness of atomoxetine for the treatment of Oppositional Defiant Disorder (ODD) comorbid with ADHD.

Method: Patients were randomly assigned (in a 2:1 ratio) to receive 1.2 mg atomoxetine (*N*=156) or placebo (*N*=70) for 8 weeks. Treatment effect on ODD and ADHD symptoms was measured using the investigator-rated Swanson, Nolan and Pelham Rating Scale-Revised (SNAP).

Results: At randomization, patient demographics and symptom severity were similar in both groups (SNAP oppositional subscale mean [SE]: baseline: atomoxetine 18.9[2.3], placebo 18.9[2.4]). Using a repeated-measures analysis, atomoxetine was superior to placebo in reducing ODD symptoms over time (*P*=.010). Secondary analyses showed, however, significant pair-wise treatment group differences at Weeks 2 and 5, but not at Week 8 postbaseline (SNAP oppositional subscale mean [SE]: Week 2: atomoxetine 15.4[0.40], placebo 17.5[0.59]; *P*=.003; Week 5: atomoxetine 15.4[0.40], placebo 16.8[0.59]; *P*=.043; Week 8: atomoxetine 15.6[0.41], placebo 16.5[0.59]; *P*=.209). An LOCF analysis indicated atomoxetine was superior to placebo at reducing ADHD symptoms (SNAP combined ADHD subscale mean change [SD]: atomoxetine −9.61[11.4], placebo −4.35[8.4]; *P*<.001).**Conclusions:** Atomoxetine significantly improved ODD symptoms in ADHD patients, but these results must be interpreted carefully because of the convergence of treatment- and placebo-group scores.

References:

1. Kuhne M, Schachar R, Tannock R: Impact of comorbid oppositional or conduct problems on attention-deficit hyperactivity disorder. 1997 J Am Acad Child Asolesc Psychiatry 36(12):1715-1725.
2. Swanson J: School-based assessments and interventions for ADD. 1992 Irvine: KC Publishing p. 184.

NR628 Wednesday, May 24, 12:00 PM - 2:00 PM

Aripiprazole or Ziprasidone to Treat Aggression in Youth

Leo J. Bastiaens, M.D. *Family Services of Western PA, 33 Sunnyhill Drive, Pittsburgh, PA, 15228*

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that both Aripiprazole and Ziprasidone are effective and safe in the short term treatment of aggression in youth.

Summary:

Objective: To evaluate the real-world effectiveness of Aripiprazole (ARI) and Ziprasidone (ZIP) in treating aggressive behavior in youth.

Methods: This is an open, non-randomized trial in a community clinic population. Patients were diagnosed with the Mini International Neuropsychiatric Interview and the Child/Adolescent Symptom Inventory. The primary outcome measure consisted of the different types of aggressive behaviors, in the past 2 weeks, endorsed by the parent, on the Overt Aggression Scale (OAS). Other measures included the Parent Young Mania Rating Scale (PYMRS), and the Health And Life Functioning Scale (HALFS/ quality of life scale). Patients with significant aggressive behavior were started on ARI (n=24) or ZIP (n=22), and followed for two months.

Results: Fourty-six patients (36 males, 40 caucasian) with a mean age of 11.9+/-2.6 (range: 6 to 17) were treated. The following disorders were the primary diagnoses: Conduct n=14; Bipolar n= 12; Mood D. NOS n=8; Psychotic n=4, Dysthymic n=4; Major Depressive n=2; Pervasive Developmental n=2. Baseline measures were as follows: OAS=7+/-1.8; PYMRS=22.6+/-8.0, HALFS 9.4+/-3.4. After 2 months, 34 patients were still in treatment with an average dose of ARI of 4.5+/-2.3 mg (n=20) and ZIP of 42.9+/-18.0 mg (n=14). AOS dropped to 2.6+/-2.5 (63 % improvement); PYMRS dropped to 9.4+/- 7.5 (58% improvement); HALFS increased to 12.8+/-3.8 (36% improvement). Clinical Global Impression-Improvement Scale was 2.1+/-1.2 (much improved). Four patients dropped out and 8 discontinued because of sedation (2 ARI; 6 ZIP). Twenty-four of 34 completers experienced side effects, mostly sedation (n=16) and dizziness (n=6). Completers gained an average of 3.2% of body weight (n=22). Neither at baseline, nor at 2 months, were there any statistically significant differences between the ARI and ZIP groups.

Conclusions: ARI and ZIP appear remarkably effective in the real-world treatment of aggressive youth. Most common side effect, at times leading to discontinuation, was sedation.

References:

1. Patel N, Crismon L, Hoagwood K, Jensen P: Unanswered questions regarding atypical antipsychotic use in aggressive children and adolescents. J Child Adolesc Psychopharm 2005; 15: 270-284.

2. Bambauer K, Connor D: Characteristics of aggression in clinically referred children. CNS Spectrums 2005; 10: 709-718.

NR629 Wednesday, May 24, 12:00 PM - 2:00 PM

Open-Label Trial of Aripiprazole in Children and Adolescents With Bipolar Disorder

Joseph Biederman *Massachusetts General Hospital, 55 Fruit Street, Warren Building 705, Boston, MA, 02114*, Eric Mick, Janet Wozniak, M.D., Paul Hammerness, M.D., Robert L. Doyle, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should recognize the treatment implications of the study, showing that open-label aripiprazole treatment is associated with a very high response rate for manic symptoms but with a modest antidepressant effect.

Summary:

Background:
The purpose of this study was to evaluate the safety, tolerability and effectiveness of aripiprazole monotherapy in the treatment of youth with bipolar disorder. Based upon the mechanism of action, we hypothesized that aripiprazole will be a well tolerated and efficacious treatment for youth with bipolar disorder.

Methods:
This was an eight-week, open-label, prospective study of aripiprazole monotherapy (7.6±3.5 mg/d) in 10 bipolar youth (manic, mixed, or hypomanic; 6-17 years old). Assessments included the Young Mania Rating Scale (YMRS), Clinical Global Impressions-Improvement scale (CGI-I), and Child Depression Rating Scale (CDRS). Adverse events were assessed through spontaneous self-reports, vital signs weight monitoring, and laboratory analysis.

Results:
Eight of the 10 youth (80%) completed the study. Aripiprazole treatment was associated with clinically and statistically significant improvement in mean YMRS scores (-15.7±9.1, p=0.0001). Using predefined criteria for improvement (Clinical Global Impressions Improvement -Mania score of ≤2 at endpoint), the response rate for manic symptoms was 90% and for symptoms of depression was 30%. The most commonly reported adverse effects were sedation (60%), extrapyramidal symptoms (30%), and anxiety (20%) From baseline to endpoint there was a statistically significant increase in weight of 1.8±0.2 kg (p=0.001).

Conclusions:
Open-label aripiprazole treatment was associated with a very high response rate for manic symptoms but with a modest antidepressant effect. Future placebo-controlled, double blind studies of the treatment of mania in youth with bipolar disorder are warranted.

References:

1. Biederman J, Faraone SV, et al.: Further evidence of unique developmental phenotypic correlates of pediatric bipolar disorder. J Affective Disorders 2004; 82(1):S45-S58.

2. Biederman J, McDonnell MA, Wozniak J, Spencer R, Aleardi M, Falzone R, Mick E: Aripiprazole in the treatment of pediatric bipolar disorder: A systematic chart review. CNS Spectrum 2005; 10:141-8.

NR630 Wednesday, May 24, 12:00 PM - 2:00 PM

Developmental Trajectories of Anxiety Disorders in Offspring at High Risk for Panic Disorder

Joseph Biederman, M.D. *Massachusetts General Hospital, Pediatric Psychopharmacology, 55 Fruit Street, Warren Building 705, Boston, MA, 02114*, Carter Petty, M.S., Dina Hirshfeld-Becker, Ph.D., Aude Henin, Ph.D., Stephen V. Faraone, Ph.D., Brianne Henry, B.A., Jerrold F. Rosenbaum

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that the risk for panic disorder is suggested to be heterogeneous and that separation anxiety disorder may help identify a group of children at very high risk for a wide range of adverse psychopathological outcomes.

Summary:

Objective. The main aim of this study was to examine whether developmental trajectories towards the development of pediatric panic disorder are operant in children at high risk for panic disorder. Based on the prior literature we hypothesized that separation anxiety disorder would be a potent predictor of subsequent panic disorder in children at risk.

Methods. We analyzed data from our large, five-year longitudinal follow-up study of well-characterized children at high and low risk for panic disorder. We compared the course of psychiatric disorders in offspring of parents with panic disorder. For the purpose of this analysis we used 95 parents with panic disorder and their 186 offspring.

Results. One hundred twenty (65%) of the high-risk offspring of parents with panic disorder had at least one anxiety disorder and 86 (46%) had two or more anxiety disorders. Separation anxiety disorder significantly increased the risk for the subsequent development of agoraphobia, GAD, panic disorder, and major depression. Agoraphobia selectively increased the risk for subsequent panic disorder and GAD selectively increased the risk for subsequent social phobia.

Conclusions. This large five-year prospective follow-up study of children at risk growing up provides compelling evidence for divergent risks conferred by specific anxiety disorders in childhood. The findings suggest that the risk for panic disorder is heterogeneous. They also indicate that separation anxiety disorder may help identify a group of children at very high risk for a wide range of adverse psychopathological outcomes.

References:

1. Biederman J, Petty C, Faraone S, Hirshfeld-Becker DR, Henin A, Rauf A, et al (2005): Childhood antecedents to panic disorder in referred and non referred adults. J Child Adolesc Psychopharmacol 15:549-562.

2. Weissman MM, Leckman JF, Merikangas KR, Gammon GD, Prusoff BA (1984): Depression and anxiety disorders in parents and children: Results from the Yale Family Study. Arch Gen Psychiatry 41:845-852.

NR631 Wednesday, May 24, 12:00 PM - 2:00 PM

Improvements in Symptoms of ADHD in School-Aged Children With Lisdexamfetamine (SPD489/NRP104) and Extended-Release Mixed Amphetamine Salts Versus Placebo

Joseph Biederman *Massachusetts General Hospital, 55 Fruit Street, Warren Building 705, Boston, MA, 02114*, Samuel Boellner, Ann Childress, Frank A. Lopez, Suma Krishnan, Paul Hodgkins

Educational Objectives:

At the conclusion of this activity, participants should be able to describe symptom improvements in children with attention-deficit/hyperactivity disorder (ADHD) after treatment with lisdexamfetamine dimesylate (SPD489/NRP104), an amphetamine prodrug, composed of d-amphetamine with an L-lysine conjugate that needs to be hydrolyzed to release the active component, and extended-release mixed amphetamine salts (MAS XR), compared with placebo.

Summary:

Objective: To compare the efficacy and safety of lisdexamfetamine dimesylate, which may have a reduced abuse potential compared to other amphetamine products, and MAS XR with placebo in school-aged children with ADHD.

Methods: Phase 2, multicenter study conducted in an analog classroom environment, comparing lisdexamfetamine (30, 50, or 70 mg) and MAS XR (10, 20, or 30 mg) with placebo, in children (6-12 years) with ADHD who had been treated with a stimulant for ≥1 of the past 6 months. There was a 1-week screening phase, a 3-week MAS XR dose optimization phase, and a randomized, double-blind, 3-week, 3-way crossover, with subjects receiving 1 week each of lisdexamfetamine (dose equivalent to subject's optimal MAS XR dose), MAS XR (subject's optimal dose), or placebo. Efficacy measures included the SKAMP and PERMP. Safety parameters included AEs, vital signs, and ECGs.

Results: 52 subjects were enrolled and 50 completed the study; 2 terminated during the first double-blind treatment week while on placebo. Least squares (LS) mean SKAMP-deportment scores significantly and comparably improved with both active treatments (lisdexamfetamine, 0.8; MAS XR, 0.8) versus placebo (1.7) (P<0.0001, for both). Significant improvement in the LS mean PERMP-attempted (lisdexamfetamine, 133.3; MAS XR, 133.6; placebo, 88.2 [P<0.0001, for both]) and PERMP-correct (lisdexamfetamine, 129.6; MAS XR, 129.4; placebo, 84.1 [P<0.0001, for both]) was also seen with both active treatments versus placebo. AEs were mild to moderate in severity, with no notable vital signs or changes in ECG parameters with the active treatments. The most common AEs for lisdexamfetamine were insomnia (8%), decreased appetite (6%) and anorexia (4%); for MAS XR they were decreased appetite (4%), upper abdominal pain (4%), insomnia (2%), and vomiting (2%).

Conclusions: Lisdexamfetamine and MAS XR resulted in comparable, significant improvements in ADHD symptom control versus placebo and were well tolerated in school-aged children with ADHD.

References:

1. Stockl KM, Hughes TE, Jarrar MA, Secnik K, Perwien AR. Physician perception of the use of medications for attention deficit hyperactivity disorder. J Manag Care Pharm. 2003;9:416-423.
2. Wigal SB, Gupta S, Guinta D, Swanson JM. Reliability and validity of the SKAMP rating scale in a laboratory school setting. Psychopharmacol Bull. 1998;34:47-53.

NR632 Wednesday, May 24, 12:00 PM - 2:00 PM

Efficacy and Safety of Lisdexamfetamine (SPD489/NRP104) in Children Aged 6 to 12 Years With ADHD

Joseph Biederman *Massachusetts General Hospital, 55 Fruit Street, Warren Building 705, Boston, MA, 02114*, Paul Hodgkins, Suma Krishnan, Robert L. Findling

Educational Objectives:

At the conclusion of this presentation, participants should be able to describe the efficacy (measured by the ADHD-Rating Scale [ADHD-RS]) and safety of lisdexamfetamine dimesylate (SPD489/NRP104), an amphetamine prodrug, composed of d-amphetamine with an L-lysine conjugate that needs to be hydrolyzed to release the active component, in children with attention-deficit/hyperactivity disorder (ADHD) compared with placebo.

Summary:

Objective: To compare the efficacy and safety of lisdexamfetamine, which may have a reduced abuse potential compared to other amphetamine products, with placebo in school-aged children with ADHD.

Methods: Phase 3, randomized, multicenter, double-blind, parallel-group study with children (6-12 years) with ADHD (either combined or hyperactive-impulsive subtypes), whether or not on medication for ADHD. The study consisted of one week to screen subjects, a one-week washout, and four weeks for the double-blind treatment. Subjects were randomized in a 1:1:1:1 ratio to a single daily dose of lisdexamfetamine (30, 50, or 70 mg) or placebo. The primary efficacy measure was the ADHD Rating Scale (ADHD-RS). Safety parameters included AEs, vital signs, laboratory tests, and ECGs.

Results: Of the 290 randomized subjects, 230 (in brackets) completed the trial (placebo n=72 [54]; lisdexamfetamine 30 mg n=71 [56]; 50 mg n=74 [60]; 70 mg n=73 [60]). The most common reasons for discontinuations were lack of efficacy (placebo, 17%; 30 mg, 1%; 50 mg, 0%; 70 mg, 1%) and AEs (placebo, 1%; 30 mg, 9%; 50 mg, 5%; 70 mg, 14%). There were no notable demographic differences between groups, with 36% of the subjects previously treated for ADHD. At study end, the ADHD-RS changes from baseline were -6.2, -21.8, -23.4, and -26.7 for placebo, lisdexamfetamine 30 mg, 50 mg, and 70 mg, respectively. Significant improvements in ADHD symptoms were seen with all doses of lisdexamfetamine compared with placebo (P<0.0001). Significant differences for all doses of lisdexamfetamine versus placebo were observed as early as week 1 (P<0.0001 for all comparisons). Most AEs were mild to moderate in severity and occurred in the first week. The most common AEs were decreased appetite, insomnia, headache, and upper abdominal pain.

Conclusions: In children with ADHD, short-term treatment with lisdexamfetamine significantly improved ADHD symptoms and was well tolerated.

References:

1. Dulcan M. Practice parameters for the assessment and treatment of children, adolescents, and adults with attention-deficit/hyperactivity disorder. J Am Acad Child Adolesc Psychiatry. 1997;36(10 suppl):85S-121S.
2. Stockl KM, Hughes TE, Jarrar MA, Secnik K, Perwien AR. Physician perception of the use of medications for attention deficit hyperactivity disorder. J Manag Care Pharm. 2003;9:416-423.

NR633 Wednesday, May 24, 12:00 PM - 2:00 PM

Parent Methamphetamine Abuse and Rural Children: A Mixed-Methods Study

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to:

1. Demonstrate knowledge of the basic epidemiology of methamphetamine abuse in the rural U.S.
2. Recognize the social and psychological impact of parent methamphetamine abuse on children.
3. Recognize the grief/loss issues embedded in foster care secondary to parental substance abuse.

4. Formulate appropriate mental health intervention goals for children with similar abuse and neglect histories.

Summary:

Over the last decade the abuse of "crystal meth", a new recipe for inexpensive and smokable methamphetamine, has become a growing and urgent problem across the United States and other countries. The addiction hits hard and fast enough to profoundly impair parenting.

Objectives: This mixed-methods study examined the mental health status and perspectives of rural school-aged foster children in the Midwest USA who were exposed to parent methamphetamine abuse.

Methods: Eighteen children who were exposed to parent methamphetamine abuse participated. Mental health status was derived from the Child Behavior Checklist and the Trauma Symptom Checklist. A semi-structured, individual interview provided information on children's perspectives on parent methamphetamine abuse and related family experiences. Additional information on children's mental health came from reviewing available records.

Results: Per foster parent report, fifty percent of children were evidencing significant emotional or behavioral problems. Children themselves underreported mental health problems. They did report avoidant or passive coping skills and noted they felt isolated or unheard in their families. Talking to others was seen by some children as taboo. Children reported issues of loss and grief much more than adults.

Conclusions: Mental health service providers should be alert to the complexities in assessing the mental health needs of children reared by parents who abuse methamphetamine. Because some children have not had support for talking about experiences and feelings or believe that talking to others is taboo, helping children to acknowledge their feelings and experiences is likely to be a key part of any intervention.

References:

1. Haight, WL, Jacobsen T, Black J, Kingery L, Sheridan K, & Mulder C: â† In these bleak daysâ‡: Parent methamphetamine abuse and child welfare in the rural Midwest. Child Youth Serv Rev 2005; 27: 949-971.
2. Cretzmeyer M, Sarrazin MV, Huber, DL, Block RI, & Hall JA: Treatment of methamphetamine abuse: Research findings and clinical directions. J Substance Abuse Treatment 2003, 24: 267-277.

NR634 Wednesday, May 24, 12:00 PM - 2:00 PM

Quetiapine Monotherapy in Patients With GAD

Olga Brawman-Mintzer, M.D. *Medical University of South Carolina, Psychiatry and Behavioral Sciences, 5900 Core Road, Suite 203, Charleston, SC, 29406*, Paul J. Nietert, Ph.D., Moira A. Rynn, M.D., Karl Rickels, M.D.

Educational Objectives:

Educational objective: At the conclusion of this presentation, the participant should understand the benefits of quetiapine in the treatment of patients with GAD

Summary:

Objective: Atypical antipsychotics have demonstrated potential efficacy as augmenting agents in treatment-resistant GAD. This double-blind, placebo-controlled trial assessed the efficacy of quetiapine monotherapy in GAD.

Methods: Thirty-eight, non-depressed GAD patients (HAM-A total score >20) were randomized, following a one-week placebo run-in, to 6 weeks of double-blind treatment with quetiapine (25-300 mg/day) or placebo (assessments at Weeks 1, 2, 4, and 6). Primary efficacy variable was defined as change from baseline in HAM-A total score. Response (>50% reduction in HAM-A total score) and remission (HAM-A total score ≤7) rates were also assessed. Safety assessments included AIMS, SAS, BAS and AEs monitoring.

Results: 12/19 quetiapine and 16/19 placebo patients completed treatment. Quetiapine (mean endpoint dose 125 mg/day) significantly reduced HAM-A total and psychic subscale scores at Weeks 2 and 4 compared with placebo in OC analyses ($p<0.05$). However, statistical significance was not sustained to endpoint (week 6), or in the LOCF sample analysis. Response (57.9% versus 36.8%) and remission (42.1% versus 21.1%) rates were numerically higher with quetiapine. No significant differences were observed in AIMS, SAS, BAS or incidence of AEs (most common AEs: fatigue and somnolence).

Conclusions: Quetiapine may represent a treatment option for patients with GAD. Additional studies are warranted to further characterize the efficacy of quetiapine in these patients.

References:

1. Brawman-Mintzer O, Knapp R, Nietert P: Adjunctive risperidone in generalized anxiety disorder: a double-blind, placebo-controlled study. J Clin Psychiatry. 2005; 66:1321-1325.
2. Pollack MH, Simon NM, Zalta AK, Worthington JJ, Hoge EA, Mick E, Kinrys G, Oppenheimer J. Olanzapine augmentation of fluoxetine for refractory generalized anxiety disorder: a placebo controlled study. Biol Psychiatry. 2005 Aug 31; [Epub ahead of p.

NR635 Wednesday, May 24, 12:00 PM - 2:00 PM

Parent and Teacher Rated Effects of MTS and OROS Methylphenidate in ADHD

Oscar G. Bukstein, M.D. *Western Psychiatric Institute and Clinic, 3811 O'Hara Street, Pittsburgh, PA, 15213-2593*, Bradley D. Vince, D.O., Frank A. Lopez, M.D., Leon Rosenberg, M.D., Robert L. Findling, M.D., Maryann Livolsi, R.N.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to: Describe the clinical use of the methylphenidate transdermal system (MTS) in pediatric subjects. Discuss the parent-based ratings of efficacy of MTS as compared with placebo in a naturalistic setting study.

Summary:

Objective: Evaluate the efficacy of a methylphenidate transdermal system (MTS), compared with placebo, using OROS methylphenidate as a reference therapy, and using parent and teacher ratings in a naturalistic community setting.

Method: This was a randomized, double-blind, parallel-group, placebo-controlled study with a 5-week dose optimization phase. Children aged 6-12 years diagnosed with ADHD by DSM-IV-TR criteria were enrolled. Parent-rated efficacy measures included the Conners' Parent Rating Scale-Revised: Short Form (CPRS-R), administered at 11:00am and 3:00pm on the last weekend day prior to study visits. CPRS-R subscales for ADHD index, oppositional, hyperactivity, and cognitive problems were used to assess efficacy and behavior. The Conners' Teacher Rating Scale-Revised: Short Form (CTRS-R) was administered at 10:00am and 2:00pm on two days (at least 48 hours apart) each study week.

Results: The change from baseline in CPRS-R scores at the 11:00am time point was statistically significant for MTS treatment compared with placebo for the ADHD index ($p=0.0002$), oppositional ($p<0.02$), hyperactivity ($p<0.0001$), and cognitive problems ($p=0.0001$) subscales. At the 3:00pm time point, change from baseline was statistically significant for MTS compared with pla-

cebo for the ADHD index (p=0.0001), hyperactivity (p<0.0001), and cognitive problems (p<0.0001) subscales, but not the oppositional subscale (p=0.1040). Results were similar for teacher ratings; at study endpoint, change from baseline for MTS treatment was statistically significant (p<0.0001) compared to placebo.

Conclusion: Treatment with MTS resulted in significant improvements in parent and teacher ratings of behavior compared with placebo in both the morning and afternoon. The efficacy and safety of MTS was similar to OROS methylphenidate. MTS may be an effective alternative to oral medications for the treatment of pediatric ADHD.

Supported by funding from Shire US Inc.

References:

1. Conners CK. Conners' Rating Scales - Revised: Technical Manual. New York, Multi-Health System, Inc., 1997.
2. Findling RL, Lopez FA. The effects of transdermal methylphenidate with reference to OROS methylphenidate in ADHD. Poster presented at the joint meeting of AACAP and CACAP. Toronto, ON, Canada. October 20, 2005.

NR636 Wednesday, May 24, 12:00 PM - 2:00 PM

Interim Results From a Long-Term Safety Study of MTS

Oscar G. Bukstein, M.D. *Western Psychiatric Institute and Clinic, 3811 O'Hara Street, Pittsburgh, PA, 15213-2593,* Robert L. Findling, M.D., Raun Melmed, M.D., Frank A. Lopez, M.D., Maryann Livolsi, R.N.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to: Describe the clinical use of the methylphenidate transdermal system (MTS) in pediatric subjects. Discuss long-term ratings of safety and efficacy in a naturalistic setting.

Summary:

Objective: This study was conducted to assess the long-term safety and efficacy of methylphenidate transdermal system (MTS).

Method: This was a multi-center, long-term, open-label study with a lead-in dose optimization phase. Children aged 6-12 years diagnosed with ADHD by DSM-IV-TR criteria that had previously participated in studies of MTS (N17-021), (SPD485-102), (SPD485-201) or (SPD485-302) were enrolled. Safety was primarily assessed by the occurrence of treatment-emergent adverse events, physical exams, vital signs, laboratory tests, ECGs, skin tolerance, and evaluation of sleep.

Results: At 8 months, interim data was available for 288 subjects included in the safety population. Of 623 adverse events recorded throughout the study, 97.8% were either mild or moderate in intensity. Three subjects experienced serious adverse events (contusion, ankle fracture, and syncope), all of which were determined by the investigator to be unrelated to the study medication. No deaths have been reported during the study. During the dose maintenance phase, a total of 320 adverse events were reported by 43.3% of subjects. The most commonly observed adverse events in the dose maintenance phase were decreased weight, decreased appetite, headache, and insomnia. No dose-related trends in adverse events were observed.

Conclusion: Long-term exposure to MTS, up to 8 months, was generally well tolerated. Nearly all adverse events reported were mild to moderate in intensity. The adverse events reported in this study are consistent with adverse events commonly reported for methylphenidate in the pediatric population. These results indicate that MTS may be a safe alternative treatment for ADHD in pediatric subjects.

Supported by funding from Shire US Inc.

References:

1. Wigal S, McGough JJ, Abikoff H, Turnbow JM, Posner K, and Moon E. Behavioral effects of methylphenidate transdermal system in children with ADHD. Poster presented at the joint meeting of AACAP and CACAP. Toronto, ON, Canada. October 21, 2005.
2. Pierce DM, Dixon CM, Wigal SB, and McGough JJ. Pharmacokinetics of methylphenidate transdermal system in children with attention-deficit/hyperactivity disorder. Poster presented at the joint meeting of AACAP and CACAP. Toronto, Canada. Oct. 20, 2005.

NR637 Wednesday, May 24, 12:00 PM - 2:00 PM

An Open-Label Pilot Study of Aripiprazole in PTSD

Marian I. Butterfield *Durham VA Medical Center/Duke Universtiy, 508 Fulton Street, 116A, Durham, NC, 27705,* Jennifer L. Strauss, Sandra Zinn, Ph.D., Susan O'Laughlin, B.A., Kathryn M. Connor, Jonathan R.T. Davidson, Christine Marx

Educational Objectives:

At the conclusion of this presentation the participant should be able to: 1) recognize that PTSD symptoms are in part mediated through abnormalities in several neurochemical systems, including dopaminergic and serotonergic systems. 2) recognize that aripiprazole, aquinolinone derivative that has effects in both the serotonergic and dopaminergic systems may be effective in reducing PTSD symptoms, and related psychotic and cognitive symptoms.

Summary:

Objective: To evaluate the short-term tolerance and potential efficacy of aripiprazole in PTSD across core symptoms and cognitive domains.

Methods: Ten veterans with PTSD were enrolled in this 12-week, open-label study of aripiprazole, flexibly dosed at 5 - 30mg. Research interviews were conducted at baseline, weekly for one month, and every two weeks through week 12. PTSD symptoms were assessed using the Treatment Outcome PTSD Scale (TOP-8), the Short PTSD Rating Interview (SPRINT), and the Clinician Administered PTSD Scale (CAPS). Psychotic symptoms were assessed with the Positive and Negative Syndrome Scale (PANSS). Neuropsychological domains of attention, executive function, learning, and memory were also assessed.

Results: Ten subjects (half women, mean age 51.5 years) were enrolled and eight completed the 12-week treatment trial. The drug was well-tolerated and mean dose at endpoint was 21.5 mg. The most common side effects of were; weight gain 60% (n= 6); concentration difficulties 30%, (n=3); akasthesia 20% (n=2); nausea 10% (n=1); and numbness and tingling 10% (n=1). Post-treatment, significant decreases in PTSD symptoms were observed on the CAPS total scores ($t = 2.39$, $p = 0.04$) and Cluster B symptoms ($t = 2.84$, $p = 0.02$), the TOP-8 ($t = 2.96$, $p = 0.02$) and SPRINT ($t = 4.66$, $p = 0.001$). Significant decreases were also noted on the three PANSS subscales (Positive Symptoms: $t = 4.03$, $p = 0.003$; Negative Symptoms: $t = 3.17$, $p = 0.011$; General Psychopathology: $t = 4.98$, $p = 0.001$). Significant improvements in delayed verbal recall that were observed from baseline to endpoint (p=0.03), however there were no differences on other neuropsychological measures.

Conclusions: Aripirazole may be an effective monotherapy for the treatment of PTSD. Our small sample size and lack of a placebo arm preclude a definitive conclusion, thus further studies are warrented.

References:

1. Butterfield, M. I., M. E. Becker, et al. (2001). "Olanzapine in the treatment of post-traumatic stress disorder: a pilot study." Int Clin Psychopharmacol 16(4): 197-203.
2. Hamner, M. B., R. A. Faldowski, et al. (2003). "Adjunctive risperidone treatment in post-traumatic stress disorder: a preliminary controlled trial of effects on comorbid psychotic symptoms." Int Clin Psychopharmacol 18(1): 1-8.

NR638 Wednesday, May 24, 12:00 PM - 2:00 PM

A Pilot Controlled Trial of Bupropion Versus Escitalopram in GAD

Alexander Bystritsky, M.D. *UCLA, Psychiatry, 300 Medical Plaza, Suite 2200, Los Angeles, CA, 90095*, Lauren Kerwin, B.A., Tanya Vapnik, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to treat anxiety disorders with Bupropion XL.

Summary:

Introduction: To evaluate whether Escitalopram or Bupropion XL has preferential efficacy in reducing specific symptoms of GAD. Specifically, whether subjects treated with Escitalopram would have significant decreases in symptoms related to fear while subjects treated with Bupropion XL would have significant increases in their ability to cope with fear (resilience).

Methods: This study utilized a randomized, double-blind, dose-controlled, parallel-group design. Thirty-four outpatients (mean age 36±2.56 yrs) were randomized into either Escitalopram (20mg/day) or Bupropion XL (300mg/day) treatment groups. The primary efficacy measures were the Hamilton Anxiety Rating Scale (HARS), UCLA-4D, and Self-Efficiency Scale (SES).

Results: Subjects in both groups showed a decrease in anxiety symptoms over the 12-week treatment period. Subjects treated with Bupropion XL showed a significant reduction in HARS scores compared to subjects treated with Escitalopram ($F= 7.66$, $df= 4,29$, $p< 01$). Subjects treated with Bupropion XL also showed a significant improvement in their ability to cope with fear, as indicated by a significant reduction in the SES scores indexing self-sufficiency. Both treatments were equally well tolerated.

Conclusion: Given the dearth of data about the safety and efficacy of Bupropion XL treatment for anxiety disorders, the findings from this study have important clinical implications. These results provide preliminary support for the safety and effectiveness of Bupropion XL in the treatment of GAD. It is hoped that these preliminary results will encourage further research to explore the use of Bupropion XL in treating GAD in adults.

References:

1. Ascher JA: Bupropion XL: a review of its mechanism of antidepressant activity. J Clin Psychiatry 1995; 56:395-401.
2. Emmanuel NP, Lydiard RP, Ballenger JC: Treatment of social phobia with Bupropion XL. J Clin Psychopharmacol 1991; 11:276-7.

NR639 Wednesday, May 24, 12:00 PM - 2:00 PM

Medication Persistence Among Agents That Treat ADHD, Diabetes, and Elevated Serum Cholesterol

Nathan M. Capone, Pharm.D. *Shire Pharmaceutical Inc, Global Medical Affairs, 725 Chesterbrook Blvd, Wayne, PA, 19087*

Educational Objectives:

At the conclusion of this session, participants should be able to describe similarities and differences in medication persistence observed among patients prescribed drugs used to treat attention-deficit/hyperactivity disorder, diabetes, and elevated serum cholesterol.

Summary:

Introduction: Adherence to prescribed drug regimens is low among patients diagnosed with ADHD. Whether medication persistence among patients prescribed a psychostimulant is different from that seen among patients prescribed drugs for other chronic medical diseases like diabetes and elevated serum cholesterol is unknown.

Methods: Prescription data obtained between September 2003 and November 2004 from a managed care pharmacy database (Catalina Health Resource) were analyzed to determine monthly persistence rates over 7 months for selected medications. Subjects were included in the analysis if a new prescription was filled during the observation period (no fills in the preceding 90 days) and the prescription indicated available refills. At each of 7 months thereafter, patients were defined as persistent if the current fill date was < the previous fill date + 31 days. Monthly persistence rates were obtained for psychostimulant drugs (mixed amphetamine salts extended release [MAS XR], methylphenidate modified release [MPH MR]), antidiabetic agents (rosiglitazone, insulin, insulin glargine), and statins (rosuvastatin, fluvastatin, atorvastatin).

Results: Medication persistence declined rapidly during the observation period for all agents examined. At month 2, persistence rates for MAS XR (62.8%) and MPH MR (64.2%) were similar to those seen for rosiglitazone (63.4%) and the statins (range, 62.2%-67.8%). By month 7, persistence declined to 22.9% and 23.5% for MAS XR and MPH MR, respectively. Slightly higher persistence rates were seen at month 7 with rosiglitazone (33.4%) and the statins (range, 26.0%-30.1%). Markedly lower persistence rates were seen for the insulins throughout observation; at month 7, persistence rates with insulin and insulin glargine were 22.4% and 17.6%, respectively.

Conclusions: After 7 months, persistence rates with psychostimulants are slightly lower than with the antidiabetic agent rosiglitazone and the statins.

This study was funded by Shire Pharmaceuticals Inc.

References:

1. Perwein A, Hall J, Swensen A, et al. Stimulant treatment patterns and compliance in children and adults with newly treated attention deficit hyperactivity disorder. J Manag Care Pharm. 2004;10:122-129.
2. Huser MA, Evans TS, Berger V. Medication adherence trends with statins. Adv Ther. 2005;22(2):163-171.

NR640 Wednesday, May 24, 12:00 PM - 2:00 PM

Rapid Cycles in Bipolar Children and Adolescents: Hospitalization and Treatment

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Educational Objectives:

understand the use of claims databases in the research of treatment of pediatric bipolar disorder.

Summary:

Background: Clinical literature refers to the rapid cycling in children and adolescents with Bipolar Disorder (BD). It is useful to provide data on this prevalent conception because rapid cycling in adults is associated with more hospitalizations as a more treatment-resistant picture.

Objective: The frequency of hospitalization and treatment of rapid cycles (>=4 episodes per year) in Children and adolescents (<=18 y.o.) with BD was examined using the Integrated Healthcare Information Services' (IHCIS) National Managed Care Benchmark.

Methods: The database includes medical history for more than 30 million managed care lives, from more than 35 US health, HMO, POS and PPO plans, covering eight census regions (mostly East coast) and patient demographics, including morbidity, age and gender. Over 90% of patients had medical and pharmaceutical benefits. From June 30, 2000 to July 1, 2003, a total number of 8,129 patients (<=18 y.o.) with BD were identified (using ICD-9 codes).

Results: Among children and adolescents with rapid cycles, 58.6% were females, 75.9% were between 12-17 y.o, and all had history of at least one hospitalization for any reason. Children and adolescents with rapid cycles (n=58) versus those without rapid cycles (n=8071) were differentiated in their hospitalization and treatment as follows: higher rate of hospital admission for any reason, for depression, and for medical conditions. As we expected, they also exhibited a significantly higher use of antidepressants, antipsychotics and mood stabilizers.

Conclusions: Following the adult criteria for rapid cycles, our findings support that children and adolescents with rapid cycles require more pharmacological treatment than those with non-rapid cycles.

References:

1. Carlson, G. A., and Kelly, K. L. Manic symptoms in psychiatrically hospitalized children--what do they mean? Journal of Affective Disorders (1998) 51(2):123-135.

2. Geller, B., Sun, K., Zimerman, B., Luby, J., Frazier, J., and Williams, M. Complex and rapid-cycling in bipolar children and adolescents: a preliminary study. Journal of Affective Disorders (1995) 34(4):259-68.

NR641 Wednesday, May 24, 12:00 PM - 2:00 PM

Prevalence, Correlates, and Comorbidity of *DSM-IV* GAD in Korean Adults

Hong Jin Jeon, M.D. *Seoul*, Bong-Jin Hahm, M.D., Jin-Pyo Hong, M.D., Jong-Ik Park, M.D., Jin-Yeong Kim, M.D., Hae woo Lee, M.D., Maeng Je Cho, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to demonstrate the characteristics of generalized anxiety disorder (GAD) in Korean population.

Summary:

Background: This study addressed the prevalence, correlates, and co-morbidity of DSM-IV GAD in a nationwide sample of Korean adults.

Methods: Face-to-face interviews were conducted with the Korean version of CIDI 2.1/DSM-IV (n=6,275, response rate 79.8%) from ten areas including metropolitan, mid-sized cities, and rural counties in South Korea.

Results: Prevalence of lifetime and 12-month GAD were 2.3% and 1.0%. Being female (OR = 2.9), separated or divorced (OR = 2.6), low income (OR = 2.1), and widowed (OR = 1.7) increased risk, respectively. GAD was highly co-morbid with major depression (43.2% of GAD). GAD was also co-morbid with bipolar disorder, substance use disorder and other anxiety disorders. Alcohol and nicotine use disorder were not significantly associated with GAD.

Conclusions: GAD is prevalent among Korean adults. Especially, GAD is highly associated with major depression.

References:

1. Grant BF et al.: Prevalence, correlates, co-morbidity, and comparative disability of DSM-IV generalized anxiety disorder in the USA: results from the National Epidemiologic Survey on Alcohol and Related Conditions. Psychol Med. 2005; 35:1747-1759.

2. Carter RM et al.: One-year prevalence of subthreshold and threshold DSM-IV generalized anxiety disorder in a nationally representative sample. Depress Anxiety. 2001;13(2):78-88.

NR642 Wednesday, May 24, 12:00 PM - 2:00 PM

Association Study for Synaptosomal-Associated Protein 25 (SNAP25) Polymorphism and Korean Patients With ADHD

Sang Hyuk Lee, M.D. *seongnam*, Tae Kyou Choi, M.D., Dong Ho Song, M.D., Hong Schick Lee, M.D.

Educational Objectives:

This study could demontrate the possibility of the association between SNAP-25 gene polymorphism and ADHD using two of the identified polymorphism(MnlI, DdeI) in Korean population.

Summary:

Objectives : ADHD(ADHD) is the most common childhood psychiatric disorder, affecting 5-10% of school-age children. Although the biological basis of this disorder is unknown, twin and family studies provide strong evidence that ADHD has a genetic basis involving multiple genes.

The gene for the synaptic vesicle docking fusion protein, synaptosomal-associated protein of 25 kDa (SNAP-25), has been implicated in the etiology of ADHD based on the mouse mutant strain coloboma. this neuron-irradiation induced mouse strain is hemizygous for the deletion of the SNAP-25 gene and displays spontaneous hyperactivity that is responsive to dextroamphetamine. DNA variations within or closely mapped to the SNAP-25 gene may alter the level of expression and hence may have an effect on the function of synaptic vesicle fusion and neurotransmitter release.

The aim of this study was to investigate the association between SNAP-25 gene polymorphism and ADHD using two of the identified polymorphism(MnlI, DdeI) in Korean population.

Methods : 95 ADHD patients and 102 normal controls participated in this study. the genotypes and allele frequency of the SNAP-25 polymorphism (MnlI, DdeI) between ADHD patients and control were compared

Results : In this study, there was statistical significant difference in genotype distribution of MnlI in SNAP-25 gene between patients and controls.(p=0.008) and t/t genotype is related ADHD(p=0.049) but DdeI is not exist in Korean population

Conclusion : This results suggest there may be a role of this polymorphism in ADHD. But the limit of this study is that the number of cases were small, therefore it would be premature to make any conclusions from this study concerning the role of SNAP-25 in ADHD. Further work is needed to assertain the role of SNAP-25 in ADHD

References:

1. Hawi Z, McCarron M, Kirley A, Daly G, Fitzgerald M, Gill M: No association of the dopamine DRD4 receptor(DRD4) gene polymorphism with attention deficit hyperactivity disorder(ADHD) in the Irish population. Am J Med Genet 2000;96:268-272.

2. Cook Jr EH, Stein MA, Krasowski MD, Cox NJ, Olkon DM, Kieffer JE et al: Association of attention-deficit disorder and the dopamine transporter gene. Am J Hum Genet 1995;56:993-998.

NR643 Wednesday, May 24, 12:00 PM - 2:00 PM

Valproate in Child and Adolescent Bipolar Disorder: A Comprehensive Meta-Analysis

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to

1) Summarize current results of the psychopharmacology of pediatric bipolar disorder that utilized structured interviews and

2) Review efficacy data and response rates to valproic acid in this population.

Summary:

Objective: To assess valproate efficacy on validated scales, including Young Mania Rating Scale (YMRS), in children with bipolar disorder via a review and meta-analysis of the literature. Method: A PubMed search conducted in June 2003 of literature published from 1990-2003 identified 46 reports of valproate use in patients aged ≤18 years with bipolar disorder. Nine viable studies were analyzed, based on inclusion criteria of utilizing a structured interview scale and therapeutic valproate level (results presented at the 2003 APA meeting). An updated search conducted in September 2005 identified 47 additional references, with 9 new reports meeting inclusion criteria. A total of 18 published reports were included in an updated meta-analysis. No reports including patients with comorbid seizure disorder were identified. Results: Eighteen published reports included 355 patients ≤18 years with bipolar disorder treated with valproate, alone or in combination. Analysis of these reports yielded an overall efficacy rate of 76% on validated interview scales (YMRS, Mania Rating Scale [MRS], Modified Mania Rating Scale [MMRS], Clinical Global Impression [CGI], and Overt Aggression Scale [OAS]). The mean serum valproate level across studies was 82.38 mcg/mL ± 9.17, suggesting a consistent therapeutic level. In the entire population of 355 patients, 271 (76%) achieved > 30% improvement on evaluation scales. In trials that defined response as > 50% improvement on YMRS, MRS, or MMRS, 105 of 149 patients (70%) responded. Conclusion: This meta-analysis demonstrates the potential benefits of valproate in children and adolescents with bipolar disorder without comorbid epilepsy. Results of large-scale, double-blind trials of valproate in children and adolescents with bipolar disorder would further support its use. Based on data in this meta-analysis, further investigation of valproate in this setting in well controlled trials is warranted.

Supported by Abbott Laboratories.

References:

1. Scheffer RE, Kowatch RA, Carmody T, Rush JA: Randomized, placebo-controlled trial of mixed amphetamine salts for symptoms of comorbid ADHD in pediatric bipolar disorder after mood stabilization with divalproex sodium. Am J Psyhiatry 2005;162:58-64.

2. Findling RL, McNamara NK, Gracious BL, et al: Combination lithium and divalproex sodium in pediatric bipolarity. J Am Acad Child Adolesc Psychiatry 2003;42:895-901.

NR644 Wednesday, May 24, 12:00 PM - 2:00 PM

A Randomized, Controlled, Pilot Study of Quetiapine in the Treatment of Adolescent Conduct Disorder

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Educational Objectives:

At the conclusion of this session, the participant should be able to evaluate the efficacy, safety, and tolerability of quetiapine relative to placebo in the treatment of aggression, oppositional behaviors, and conduct problems in adolescents.

Summary:

Introduction: Atypical antipsychotics are promising agents to treat excessive aggressive behaviors, oppositional and defiant symptoms, and conduct problems in adolescents.

Methods: Outpatients (12-17 years) with a primary diagnosis of conduct disorder and moderate/severe aggressive behavior were randomized to 7 weeks of double-blind, flexibly dosed quetiapine (N=9) or placebo (N=10) without concurrent psychotropic medication. Outcome measures included CGI-Severity and Improvement scales, Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q), Overt Aggression Scale (OAS), and Conduct Disorder Subscale of the Corners Parent Rating Scale (CPRS). Intent to treat differences were estimated by mixed effects models.

Results: Eight out of 9 patients receiving quetiapine (endpoint dose 300+/-168 mg/day) completed the study versus 3/10 with placebo. CGI-Severity score at Week 7 was 1.80 points lower with quetiapine than placebo (P=0.007). At endpoint, 8/9 patients receiving quetiapine were improved (CGI ≤2) compared to 1/10 with placebo. Q-LES-Q score increased 11.3 points with quetiapine and decreased 4 points with placebo (P=0.005). OAS and CPRS conduct subscale scores did not differ between the groups. Quetiapine was well tolerated. One patient developed akathisia during quetiapine treatment; no other extrapyramidal side effects occurred.

Conclusions: This 7-week pilot study suggests quetiapine may be effective and well-tolerated therapy in adolescents with conduct disorder.

Supported by funding from AstraZeneca Pharmaceuticals LP.

References:

1. Connor D, Boone R, Steingard R, Lopez I, Melloni R, Jr. Psychopharmacology and aggression: II. A meta-analysis of nonstimulant mediation effects on overt aggression-related behaviors in youth with SED. J Emot Behav Disord 2003;11:157-68.

2. Findling RL, McNamara NK, Branicky LA, Schluchter MD, Lemon E, Blumer JL. A double-blind pilot study of risperidone in the treatment of conduct disorder. J Am Acad Child Adolesc Psychiatry 2000;39(4):509-16.

NR645 Wednesday, May 24, 12:00 PM - 2:00 PM

Escitalopram for Specific Phobia: A Placebo-Controlled Pilot Study

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Educational Objectives:

To understand the effects of escitalopram in treating specific phobia

Summary:

Background: Specific phobia is the most common of all anxiety disorders and tends to start early in life, often becoming chronic over time. Individuals with specific phobia generally accommodate their lives around the phobia which can on occasion become quite impairing. Response to treatment is poorly understood, although there is evidence that cognitive-behavioral techniques can be ben-

eficial as well as pharmacologic agents with serotonergic and Gamma-aminobutyric acid ergic effects (e.g., clonazepam, paroxetine). With these considerations in mind, we conducted a placebo-controlled pilot study of escitalopram in subjects with specific phobia.

Methods: 13 subjects meeting DSM-IV criteria for specific phobia were randomly assigned to treatment with escitalopram or placebo. Treatment was initiated at 5 mg/day and titrated to a maximum dose of 20 mg/day through week 12, as tolerated and clinically indicated. Response was evaluated based on a > 50% reduction from baseline on the Main Phobia Questionnaire and the Fear Questionnaire and using CGI-I scores of < 2(much or very much improved).

Results: 13 subjects were enrolled and 12 returned for at least one post-baseline assessment, thereby providing evaluable data. Response in terms of fear, avoidance, state of main fear and specific fears ranged from 20-80% for escitalopram and 0-43% for placebo (NS). By week 12, the mean CGI improvement on escitalopram was 2.0 (much improved) versus 3.3 (minimally improved) on placebo (p<.06). The drug was well tolerated.

Conclusions: While treatment differences on the primary outcome measures were not statically significant, responses were consistently greater for escitalopram than for placebo. These findings, along with the noted clinical global improvement with drug, in this small sample suggest that the drug shows promise in specific phobia. Larger controlled trials are needed to better understand the role of escitalopram in treating specific phobia.

Funding for this study was provided by Forest Laboratories, Inc.

References:

1. Davidson JRT, Tupler LA, Potts NA: Treatment of social phobia with benzodiazepines. J Clin Psych 1994; 55(suppl 6):28-32.
2. Benjamin J, Ben-Zion IZ: Double-blind placebo-controlled study of paroxetine for specific phobia. Psychopharmacology 2000; 149:194-196.

NR646 Wednesday, May 24, 12:00 PM - 2:00 PM

Quetiapine/Sertraline Combination in PTSD

Aytul Corapcioglu Ozdemir, Prof. Dr. *Kocaeli University Med Faculty, IZMIT, TURKEY, Psychiatry Dept., Tophanelioglu Cad. Petek Sit. A5 Blok D: 9, Istanbul, 81140, Turkey*, Nese Kocabasoglu, Prof. Dr., Ilhan Yargic, Prof. Dr.

Educational Objectives:

At the conclusion of this presentation, the participant should understand the benefits of quetiapine/sertraline combination treatment in patients with PTSD.

Summary:

Objective: PTSD is a chronic psychological disorder which develops after physical, psychological or environmental trauma.[1,2] This 8-week randomized, double-blind study investigated the efficacy and tolerability of sertraline/quetiapine combination versus sertraline monotherapy in patients with PTSD.

Methods: Patients (aged 18-55 years; no previous sertraline treatment) with PTSD (DSM-IV) were randomized to sertraline (100-200 mg/day) plus quetiapine (200-750 mg/day; n=47) or sertraline plus placebo (n=47). Primary efficacy measure was change from baseline in the Clinician Rated PTSD Scale (CAPS). Adverse effects (AEs) and tolerability were assessed throughout.

Results: Combination of sertraline treatment with quetiapine (mean dose = 207 mg/day) significantly improved symptoms of PTSD, as assessed by change in CAPS total score at Week 8, compared to sertraline monotherapy (p<0.05). By Week 8, patients fulfilling criteria for positive PTSD diagnosis decreased by 94.1% with quetiapine, compared with 63% for sertraline monotherapy (p=0.016). Patients scoring ≥2 in at least one CAPS item decreased by 94.1% and 58.3% in the quetiapine and sertraline monotherapy groups, respectively. AEs in each treatment group were of mainly mild/moderate severity. The most common AEs were dry mouth and somnolence.

Conclusions: Quetiapine/sertraline combination significantly improves symptoms of PTSD compared with sertraline monotherapy. The combination treatment is well tolerated.

References

1. Tural U, Coskun B, Onder E, Corapcioglu A, Yildiz M, Kesepara C, Karakaya I, Aydin M, Extended Release ol A, Torun F, Aybar G: Psychological consequences of the 1999 earthquake in Turkey. J Trauma Stress 2004; 17:451-459
2. Zisook S, Chentsova-Dutton Y, Shuchter Sustained Release : PTSD following bereavement. Ann Clin Psychiatry 1998; 10:157-163

References:

1. Tural U, Coskun B, Onder E, Corapcioglu A, Yildiz M, Kesepara C, Karakaya I, Aydin M, Erol A, Torun F, Aybar G: Psychological consequences of the 1999 earthquake in Turkey. J Trauma Stress 2004; 17:451-459.
2. Zisook S, Chentsova-Dutton Y, Shuchter SR: PTSD following bereavement. Ann Clin Psychiatry 1998; 10:157-163.

NR647 Wednesday, May 24, 12:00 PM - 2:00 PM

A Single-Blind Prospective Study of Quetiapine for the Treatment of Mood Disorders in Adolescents at High Risk for Developing Bipolar Disorder

Melissa P. DelBello, M.D. *University of Cincinnati, College of Medicine, Division of Bipolar Disorders Research, Department of Psychiatry, 231 Albert Sabin Way, ML 0559, Cincinnati, OH, 45267-0559*, R. M. Whitsel, B.A., Caleb M. Adler, M.D., Robert A. Kowatch, M.D., Kevin Stanford, B.S., Stephen M. Strakowski, M.D.

Educational Objectives:

At the conclusion of this session, participants will be familiar with recent data on quetiapine for the treatment of mood disorders in adolescents who are at high risk for developing bipolar disorder.

Summary:

Objective: To evaluate the efficacy and tolerability of quetiapine[1,2] in the treatment of mood disorders in adolescents at elevated risk of developing bipolar disorder.

Methods: Single-blind (rater-blind), 84-day study of quetiapine (flexible dose 300-600 mg/day) in adolescents diagnosed with a mood disorder other than bipolar I disorder, a YMRS score ≥12 or CDRS-R score ≥28, and at least one parent with bipolar disorder. Primary efficacy measures were changes from baseline to endpoint in YMRS and CDRS-R scores.

Results: Twenty adolescents (mean age [SD] 14.7 [1.7] years; range 12-18 years) diagnosed with bipolar disorder not otherwise specified (11 [55%]), dysthymia (3 [15%]), bipolar II disorder (3 [15%]), cyclothymia (2 [10%]), or MDD (1 [5%]) participated. Mean YMRS and CDRS-R scores decreased significantly from baseline (YMRS 18.1 [SD 5.5], CDRS-R 38.2 [9.8]) at all assessments to endpoint (8.7 [7.9]; 27.7 [9.3]; all $P<0.001$). Five adolescents discontinued due to lack of response (1), symptom exacerbation (1), or withdrawal of consent/assent (3). Adverse events, including somnolence (55%) and headache (25%), were generally mild.

Conclusions: Quetiapine may be effective for the treatment of adolescents with mood disorders other than bipolar I disorder and at familial risk of bipolar disorder.

Supported by funding from AstraZeneca Pharmaceuticals LP.

References:

1. DelBello MP, Schwiers ML, Rosenberg HL, Strakowski SM. A double-blind, randomized, placebo-controlled study of quetia-

pine as adjunctive treatment for adolescent mania. J Am Acad Child Adolesc Psychiatry 2002;41(10):1216-1223.

2. DelBello MP, Kowatch RA, Adler CM, Stanford KE, Welge JA, Barzman DH, et al. A Double-blind Randomized Pilot Study Comparing Quetiapine and Divalproex for Adolescent Mania. J Am Acad Child Adolesc Psychiatry 2006:In Press.

NR648 Wednesday, May 24, 12:00 PM - 2:00 PM

Duration of Untreated Illness in GAD: A Poor Treatment Response Risk Factor?

bernardo dell'osso, M.D. *Dept. of Psychiatry, University of Milan, Department of Clinical Sciences "Luigi Sacco", University of Milan, Milan, Italy, via Piatti 8, Milano, 20123, Italy,* Emanuela Mundo, Michela Russo, M.D., Sara Fumagalli, M.D., Carlo Alfredo Altamura, Prof. Dr.

Educational Objectives:

At the conclusion of this presentation, the partecipant should be able to recognize the role of the duration of untreated illness (DUI), defined as the time elapsing between the onset of Generalized Anxiety Disorder (GAD) and the first adequate antidepressant treatment, on the treatment response of GAD.

Summary:

Objective: GAD has been recognized as one of the most frequent anxiety disorders. The aim of this study was to investigate the role of the duration of untreated illness (DUI), defined as the time elapsing between the onset of GAD and the first adequate antidepressant treatment, on the treatment response *Methods*: 31 DSM-IV-TR GAD patients, who gave their informed consent, were the sample studied. Patients were sub-divided into two groups, with DUI < 1 year (N=6) and with DUI > 1 year (N= 25). The main demographic, clinical, and outcome variables were compared between the two patient groups (Student's t-tests or chi-square tests). Patients were treated with antidepressants (SSRIs, SNRIs or combination) for 8 weeks at full doses, with no concomitant treatment except for stabilized doses of benzodiazepines. Treatment response was evaluated using the Clinical Global Impression rating scale (severity of illness) and compared between the two groups using ANOVA with repeated measures.

Results: No significant differences were found between the two treatment groups with respect to the main demographic and clinical variables. No differences in the treatment response were found according to the results of the ANOVA done on CGI scores (Time effect: F=166.64, p<0.0001, Group effect: F=1.658, p>0.2). *Conclusions:* Results from this preliminary study suggest that the DUI, differently from what happens with Panic Disorder, is not a major risk factor for poor treatment response to antidepressants in GAD patients.

References:

1. Altamura AC, Santini A, Salvadori D, Mundo E (2005). Duration of untreated illness in Panic Disorder: a poor outcome risk factor? Neuropsychiatric Disease and Treatment, 1(4): 345-347.

2. Lieb R, Becker E, Altamura C (2005). The epidemiology of generalized anxiety disorder in Europe. Eur Neuropsychopharmacol (4):445-52.

NR649 Wednesday, May 24, 12:00 PM - 2:00 PM

Improvement in Specific Aggressive Outbursts in Adolescents With ADHD Following Augmentation of Methylphenidate With Quetiapine

David W. Dunn, M.D. *Indiana University School of Medicine, Department of Psychiatry, 702 Barnhill Drive, Room 4300, Indianapolis, IN, 46202-5128*, William G. Kronenberger, Ph.D., Ann L. Giauque, M.S.W., Deborah E. Lafata, R.N., Laura E. Maxey, B.A.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to describe specific types of improvement seen in aggressive outbursts in adolescents with attention deficit hyperactivity disorder (ADHD) as a result of treatment with combined quetiapine and methylphenidate compared to methylphenidate in this study.

Summary:

Objective: To investigate change in specific types of aggressive outbursts during stimulant monotherapy and following addition of quetiapine to stimulant monotherapy in adolescents with ADHD and aggression.

Methods: This open-label trial investigated 3 weeks of Oros® methylphenidate monotherapy (54 mg/day) followed by 9 weeks of treatment with methylphenidate combined with quetiapine (up to 600 mg/day). Twenty-four adolescents (ages 12-16 years) with ADHD, oppositional defiant disorder or conduct disorder, and severe aggressive outbursts participated. The Modified Overt Aggression Scale was administered by a child psychiatrist or psychologist to track outbursts.

Results: No participants experienced outbursts of serious injury to self or others. Mean incidents per week of moderate self-harm (e.g. hitting walls) declined significantly (P<0.05) from 4 at study entry to 2 following stimulant monotherapy (at 3 weeks) to less than 1 with combination treatment (after 9 weeks). Mean incidents per week of moderate aggression toward others (e.g. fighting without injury) also declined significantly (P<0.05) from 3 at study entry to 1 following stimulant monotherapy and less than 1 following combination treatment. Similar declines were seen for verbal aggression and aggression toward property. Safety and tolerability analyses are reported in a separate manuscript (Kronenberger et al., under review).

Conclusions: Methylphenidate alone and combined with quetiapine produced decreases in specific aggression outbursts. The combined treatment appeared to produce an additional advantage over monotherapy for treating moderate physical and verbal aggressive outbursts.

Funding for this research was provided by AstraZeneca Pharmaceuticals LP

References:

1. Connor DF, Glatt SJ, Lopez ID, Jackson D, Melloni RH Jr. Psychopharmacology and aggression. I. A meta-analysis of stimulant effects on overt/covert aggression-related behaviors in ADHD. J Am Acad Child Adolesc Psychiatry 2002;41:253-61.

2. Patel NC, Crismon ML, Hoagwood K, Jensen PS. Unanswered questions regarding atypical antipsychotic use in aggressive children and adolescents. J Child Adolesc Psychopharmacol 2005;15:270-84.

NR650 Wednesday, May 24, 12:00 PM - 2:00 PM

Atomoxetine Treatment for ADHD: Young Adults Compared With Older Adults

Todd M. Durell, M.D. *Eli Lilly and Company, Neuroscience, 7313 Oaklandon Road, Indianapolis, IN, 46236*, Lenard A. Adler, Timothy E. Wilens, Martin Paczkowski, Kory Schuh

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize and compare the effects of atomoxetine for treating ADHD in young adults, aged 18 to 25 years, with adults older than 25.

Summary:

Objective: Atomoxetine is a nonstimulant medication for treating child, adolescent, and adult ADHD.[1,2] This meta-analysis compared the effects in young and older adults.

Methods: Patients in two identical studies received twice-daily atomoxetine or placebo for about 10 weeks. Data from patients aged 18-25 years (atomoxetine, n=26; placebo, n=29) were compared with patients older than 25 (atomoxetine, n=244; placebo, n=237). Efficacy measures included the Conners' Adult ADHD Rating Scale (CAARS) and the Clinical Global Impressions-Severity (CGI-S).

Results: In younger adults, atomoxetine produced significantly greater benefits relative to placebo as measured by mean changes from baseline on the CAARS Total ADHD Symptom Score (-11.77 versus -8.38 for atomoxetine and placebo, respectively; p=.041; effect size=.797) and the CGI-S (-0.88 versus -0.52; p=.006; effect size=1.121). In older adults, atomoxetine also produced significant benefits (CAARS Total score changes of -12.22 and -8.36; p<.001; effect size=.326; CGI-S changes of -0.95 versus -0.55; p<.001; effect size=.346). Larger effect sizes for the young adults reflect smaller variability for this group. Tolerability was generally similar between age groups although older adults reported more sexual side effects. **Conclusion:** These data indicate that atomoxetine is efficacious for treating ADHD in young adults, although this analysis has limitations due to a small sample size. Funding provided by Eli Lilly and Company.

References:

1. Michelson D, Allen AJ, Busner J, et al.,: Once-daily atomoxetine treatment for children and adolescents with attention-deficit/hyperactivity disorder: A randomized, placebo-controlled study. Am J Psychiatry 2002;159:1896-1901.
2. Kelsey DK, et al.,: Once-daily atomoxetine treatment for children with attention-deficit/hyperactivity disorder, including an assessment of evening and morning behavior: A double-blind, placebo-controlled trial. Pediatrics 2004;114(1):e1.

NR651 Wednesday, May 24, 12:00 PM - 2:00 PM

Childhood-Onset OCD Tic Disorders: Rheumatic Fever Behind the Behavioral Disorder in Children

Mohamad R. Eskandari, M.D. *Zanjan University of Medical Scienses, Psychiatry, Beheshti Hospital, Arq Square, Zanjan, 45136, Iran (Islamic Republic of)*, Soghra Karami, M.S.C.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize or have enough attention to relationship between PANDAS and sudden onset OCD and tic disorders in children. Children with sudden onset or episodic course of obsessions and compulsions, and tics with recent history of pharyngitis should be checked for having RF and PANDAS. The rates of tic disorders and OCD in first-degree relatives of children with PANDAS are higher than those reported in the general population.

Summary:

Background: Psychiatric symptoms such as obsessions, compulsions and tics in children may lead a psychiatrist to important diagnoses such as Rheumatic fever (RF) and Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal infections (PANDAS) in children. The aim of this study is to evaluate clinical characteristics of RF and PANDAS in a group of children that referred as behavioral problems.

Methods: Children with sudden onset or episodic course of obsessions and compulsions, and tics were included in this study. 36 children aged 5-12 referred with sudden onset or episodic course of behavioral problems who were assessed as having RF and/ or PANDAS by Jones Criteria and/ or PANDAS criteria, laboratory tests, physical examination, and psychiatric interview.

Results: 17 children (47.2 %) had criteria as RF and/or PANDAS. 16 %(6 of 36) diagnosed by Jones Criteria to have RF and 30.5 % (11 of 36) diagnosed to have PANDAS (36.3 % (N=4) with diagnosis of OCD, 45.5 %(N=5) with diagnosis of a tic disorder and 18.1 % (N=2) with mixed diagnosis of OCD and tic disorder.) All of the children (100%) with RF diagnosis were in Sydenham's chorea (SC) phase and had irritability, obsessions and compulsions, and tics. 83.3 % (5 of 6) of affected children had at least one affected first degree-relative with tic disorders and/ or obsessive compulsive disorders.

Conclusion SC is a major manifestation of RF and some of the same symptoms are seen in OCD and tic disorders. The rates of tic disorders and OCD in first-degree relatives of children with PANDAS are higher than those reported in the general population. Children with sudden onset or episodic course of obsessions and compulsions, and tics with recent history of pharyngitis should be checked to having RF and PANDAS.

References:

1. Snider LA, Swedo SE: Childhood-onset obsessive-compulsive disorder and tic disorders: case report and literature review. J Child Adolesc Psychopharmacol. 2003;13 Suppl 1:S81-8.
2. Swedo SE, Leonard HL, Rapoport JL: The Pediatric Autoimmune Neuropsychiatric Disorders Associated With Streptococcal Infection (PANDAS) Subgroup: Separating Fact From Fiction Peditrics Vol. 113 No. 4 April 2004, 907-911.

NR652 Wednesday, May 24, 12:00 PM - 2:00 PM

Comparing the Efficacy of Medications for ADHD Using Meta-Analysis

Stephen V. Faraone, Ph.D. *SUNY Upstate Medical University, 750 East Adams St, Syracuse, NY, 13210*

Educational Objectives:

At the conclusion of this session, participants should be able to describe the attention-deficit/hyperactivity disorder drug-placebo variability through effect size comparison.

Summary:

Introduction: Although the medications used to treat ADHD have been well researched, comparisons between them are hindered by the absence of direct comparative trials. Moreover, little is known about how study design features influence estimates of effect size. We analyzed recent published literature on the pharmacotherapy of ADHD to examine these issues and to describe the variability of drug-placebo effect sizes.

Methods: A literature search was conducted to identify double-blind, placebo-controlled treatment studies of ADHD youth published during or after 1980. Meta-analysis regression assessed the influence of medication type and study design features on medication effects. Sixty trials met criteria and were included in this meta-analysis. These trials studied 21 drugs using 40 different outcome measures of hyperactive, inattentive, impulsive, or oppositional behavior. The most commonly identified treatments included both methylphenidate and amphetamine compounds.

Results: After stratifying trials on the class of drug studied (nonstimulant versus stimulant versus long-acting stimulant), we found significant drug differences for both study design variables and effect sizes. The differences among the 3 drug classes remained significant after correcting for study design variables. There does not appear to be uniformity in how medication effectiveness is assessed or in many study design parameters. Comparing medication effect sizes from different studies will be biased if variability in study design parameters is not accounted for.

Conclusions: Although these differences obscure comparisons between specific medications, they do allow for conclusions about the differential effects of medications used to treat ADHD.

This study was funded by Shire Pharmaceuticals Inc.

References:

1. Faraone SV, et al. Meta-analysis of the efficacy of methylphenidate for treating adult attention-deficit/hyperactivity disorder. J Clin Psychopharmacol. 2004;24:24-29.
2. Faraone SV. Understanding the effect size of ADHD medications: implications for clinical care. Medscape Psychiatry & Mental Health. 2003;8.

NR653 Wednesday, May 24, 12:00 PM - 2:00 PM

Efficacy of Aripiprazole in Children and Adolescents With Major Psychiatric Diagnoses

Robert L. Findling, M.D. *Case Western University, 11100 Euclid Avenue, Suite 200, Cleveland, OH, 44106-5080*, Philippe Auby, M.D., Margaretta Nyilas, M.D., Suresh Mallikaarjun, Ph.D., Robert A. Forbes, Ph.D., Ronald Marcus, M.D., William H. Carson, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant will be aware of the effective dose range of aripiprazole 1-30 mg in children and adolescents with major psychiatric disorders.

Summary:

Objectives: These two studies examined the efficacy and tolerability of aripiprazole 1-30 mg in children and adolescents (6-17 years) with major psychiatric diagnoses.

Methods: *Study 1 (1-15 mg)*: Open-label, 15-day, 3-center, fixed-dose trial. 23 children and adolescents (6-17 years) with a diagnosis of conduct disorder were enrolled. Dosing was based on body weight: <25 kg received 1 mg, 25-50 kg received 2 mg, 50-70 kg received 5 mg, and >70 kg received 10 mg (one patient received 15 mg). *Study 2 (20-30 mg):* Open-label, 26-day, multicenter, sequential cohort, dose-escalation trial. 19 children and adolescents (10-17 years) were enrolled. Preferential enrollment was given to patients with schizophrenia or bipolar illness; however, other psychiatric diagnoses were also permitted. 57% of patients were diagnosed with bipolar disorder; 38%, Tourette's disorder; and 4%, schizophrenia. All patients started on a dose of aripiprazole 2 mg/day. Three cohorts reached final doses of 20 mg, 25 mg, or 30 mg/day over a maximum of 12 days, and maintained that dose for an additional 14 days. Efficacy was assessed using the Rating of Aggression Against People and/or Property (RAAPP) (Study 1 only), CGI-Severity, and CGI-Improvement.

Results: Baseline CGI-S was 3.9 (moderately ill) and showed clinically meaningful improvement by an average decrease of 1.7 points (2.2; borderline mentally ill) over the course of the two studies. 71% (29/41) of patients from both studies were "very much improved" or "much improved" at study endpoint, as measured by the CGI-I. RAAPP scores (Study 1) improved from moderate severity to mild severity at study endpoint.

Conclusions: Effectiveness of 1-30 mg/day is demonstrated in this patient population. Improvement of symptoms suggests that aripiprazole should be systematically evaluated in pediatric/adolescent disorders.

References:

1. Burris KD, Molski TF, Xu C: Aripiprazole, a novel antipsychotic, is a high affinity partial agonist at human dopamine D2 receptors. J Pharmacol Exp Ther. 2002; 302:381-389.
2. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, 282.

NR654 Wednesday, May 24, 12:00 PM - 2:00 PM

Pharmacokinetics and Tolerability of Aripiprazole in Children and Adolescents With Major Psychiatric Diagnoses

Robert L. Findling, M.D. *Case Western University, 11100 Euclid Avenue, Suite 200, Cleveland, OH, 44106-5080*, Philippe Auby, M.D., Margaretta Nyilas, M.D., Suresh Mallikaarjun, Ph.D., Robert Forbes, Ph.D., Ronald Marcus, M.D., William H. Carson, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant will know that the pharmacokinetics of aripiprazole in children and adolescents are linear and similar to that observed in adults; and that doses of aripiprazole 1-30 mg were generally well tolerated without regard to body weight, gender, or psychiatric disorder.

Summary:

Objectives: These two studies examined the pharmacokinetics and tolerability of aripiprazole 1-30 mg in children and adolescents.

Methods: *Study 1 (1-15 mg)*: Open-label, 15-day, 3-center, fixed-dose trial. 23 children and adolescents (6-17 years) with a diagnosis of conduct disorder were enrolled. Dosing was based on body weight: <25 kg received 1mg, 25-50 kg received 2 mg, 50-70 kg received 5 mg, and >70 kg received 10 mg (one patient received 15 mg). *Study 2 (20-30 mg):* Open-label, 26-day, multicenter, sequential cohort, dose-escalation trial. 19 children and adolescents (10-17 years) were enrolled. Preferential enrollment was given to patients with schizophrenia or bipolar illness; however, other psychiatric diagnoses were permitted. All patients were gradually titrated from a starting dose of 2 mg/day, to final doses of 20 mg, 25 mg, or 30 mg/day over a maximum of 12 days. Final doses were maintained for 14 days. *Patient Assessment (Studies 1 and 2):* Tolerability/safety was assessed based on spontaneously reported adverse events, ECGs, vital signs, clinical lab values, physical exam, and EPS rating scales.

Results: Aripiprazole pharmacokinetics were linear across doses as assessed by steady-state oral clearance. The mean (SD) steady-state oral clearance for the 30-mg dose group [58.8 (27.7) mL/h/kg] is similar to that reported for adult patients in another study 52.0 (30.7) mL/h/kg. Tmax (median) ranged from 2-4 hours across dose groups. Aripiprazole was generally well tolerated in both studies. Most commonly reported adverse events (headache, vomiting, somnolence, lightheadedness) were mild and transient in nature, with no relationship to dose. One patient discontinued due to acute dystonia.

Conclusions: Doses of 1-30 mg/day are generally well tolerated in children in adolescents, without regard to body weight, gender, or psychiatric diagnosis. Pharmacokinetics are linear and similar to that observed in adults.

References:

1. Burris KD, Molski TF, Xu C: Aripiprazole, a novel antipsychotic, is a high affinity partial agonist at human dopamine D2 receptors. J Pharmacol Exp Ther. 2002; 302:381-389.
2. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, 282.

NR655 Wednesday, May 24, 12:00 PM - 2:00 PM

The Aberrant Behavior Checklist: Use in Clinical Trials of Pediatric Autism

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to (1) discuss the use of the Aberrant Behavior Checklist as an outcome measure in pediatric autism trials and (2) discuss the correlation between the ABC and recommended measures of core autism symptoms and global condition.

Summary:

Objective: This subanalysis examined whether the Aberrant Behavior Checklist (ABC)[1] correlates with measures of core autism symptoms (Childhood Autism Rating Scale [CARS]) and global clinical condition.

Methods: We evaluated a subpopulation of children (5-12 years) with autism and a baseline CARS score ≥30 (n=55) enrolled in an 8-week, randomized, double-blind, placebo-controlled trial of risperidone (0.01-0.06 mg/kg/day) for pervasive developmental disorders.[2] Pearson's correlations between ABC total and subscale scores and CARS subscale scores, and the Clinical Global Impression-Severity (CGI-S) at baseline, or the CGI-Change (CGI-C) score at all visits were calculated.

Results: At baseline, 6 of the 15 CARS subscales (II-imitation, IV-body use, V-object use, VI-adaptation to change, XI-verbal communication, XIII-activity level) showed a significant positive correlation with 1 or more of the ABC subscales, with the strongest correlation observed for ABC-stereotypic behavior and CARS-imitation (r=0.444; *P*=0.001; n=53). ABC total scores showed a positive correlation with CARS subscales II, V, XIII (*P*<0.05 for each). At baseline, there were no significant positive correlations between the CGI-S and ABC scores.

At all visits, there was a significant correlation between ABC total scores and CGI-C scores, which increased to r=0.555 at endpoint (*P*<0.0001; n=53). Few significant correlations were observed between CARS baseline scores and ABC subscale scores over time. **Conclusions:** In this population, baseline severity of 6 CARS symptoms correlated to baseline ABC subscales. During the trial, ABC scores correlated well with change in global condition over time, indicating that the ABC score is sensitive to pharmacological treatment effects in children with autism. However, there were few significant correlations between CARS baseline scores and changes over time on ABC subscales, which suggests the ABC may be sensitive to treatment effects irrespective of the baseline severity of autistic symptoms. Supported by Janssen, L.P.

References:

1. Aman M, Singh N, Stewart A, Field C. The aberrant behavior checklist: a behavior rating scale for the assessment of treatment effects. Am J Ment Defic. 1985;89:485-91.
2. Shea S, Turgay A, Carroll A, Schulz M, Orlik H, Smith I, et al. Risperidone in the treatment of disruptive behavioral symptoms in children with autistic and other pervasive developmental disorders. Pediatrics. 2004;114:e634-41.

NR656 Wednesday, May 24, 12:00 PM - 2:00 PM

Dissociative Symptoms and History of Trauma Among Patients With OCD and Social Anxiety Disorder

Leonardo F. Fontenelle, M.D. *Institute of Psychiatry of the Federal University of Rio de Janeiro, Department of Psychiatry and Legal Medicine, Rua OtÃ,vio Carneiro 93 601 IcaraÃ, NiterÃi-RJ, 24230-190, Brazil*, Aline M. Domingues, Ph.D., Gabriela B. de Menezes, M.D., Ivan L. Figueira, M.D., Wanderson F. Souza, Ph.D., Marcio Versiani, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that dissociative symptoms may be a part of the psychopathology of obsessive-compulsive disorder and social anxiety disorder.

Summary:

Objectives: To compare the profile and severity of dissociative symptoms of patients with OCD to those of patients with social anxiety disorder (SAD). METHODS: Patients with OCD (n=29) and patients with SAD (n=19) had their diagnoses confirmed by means of the Structured Clinical Interview for DSM-IV and were examined with the following instruments: Dissociative Experience Scale (DES), Trauma History Questionnaire (THQ), Obsessive-Compulsive Inventory (OCI), Liebowitz Social Anxiety Scale (LSAS), Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI). The profile of responses of patients with OCD were compared to those of patients with SAD by means of the Student's t test and the chi-square test. Pearson's correlation analysis was performed between the DES and the THQ scores and the severity of obsessive-compulsive (OCI), phobic (LSAS), depressive (BDI) and anxiety (BAI) symptoms. Results: The severity of dissociative symptoms among patients with OCD was not significantly different from those of patients with SAD, although a trend to greater severity was found among the latter. A significant correlation was found between the severity of dissociative symptoms and the severity of phobic (r=.57, p<.001), obsessive-compulsive [specially hoarding symptoms (r=.33, p=0.02)], anxiety (r=.64, p<.001) and depressive symptoms (r=.46, p=0.001). Patients with SAD had significantly higher rates of previous exposure to crimes, disasters, and physical abuse. Conclusions: Dissociative symptoms cut across different anxiety disorders. Patients with hoarding symptoms may display increased severity of dissociative symptoms. Patients with SAD are probably more vulnerable to several types of traumatic experiences.

References:

1. Watson D, Wu KD, Cutshall C. ymptom subtypes of obsessive-compulsive disorder and their relation to dissociation. J Anxiety Disord 2004;18: 435-58.
2. Ball S, Robinson A, Shekhar A, Walsh K. Dissociative symptoms in panic disorder. J Nerv Ment Dis 1997; 185: 755-60.

NR657 Wednesday, May 24, 12:00 PM - 2:00 PM

Sexual Function and Dysfunction Among Patients With OCD and Social Anxiety Disorder

Leonardo F. Fontenelle, M.D. *Institute of Psychiatry of the Federal University of Rio de Janeiro, Department of Psychiatry and Legal Medicine, Rua OtÃ,vio Carneiro 93 601 IcaraÃ, NiterÃi, 24230-190, Brazil*, Gabriela B. de Menezes, M.D., Roberto R. Miotto, M.D., Rodrigo FalcÃ£o, M.D., Wanderson F. Souza, M.D., Marcio Versiani, M.D., Ivan L. Figueira, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that obsessive-compulsive disorder and social anxiety disorder may be associated with different profiles of sexual dysfunction.

Summary:

Objectives: In this exploratory study, our objective was to compare the history, the profile, and the severity of sexual symptoms of patients with OCD to those of patients with social anxiety disorder (SAD). Methods: Patients with OCD (n=31) and patients with SAD (n=26) had their diagnoses confirmed by means of the Structured Clinical Interview for DSM-IV and were examined with the following instruments: The Sexual Inventory of the Institute of Psychiatry of the Federal University Rio de Janeiro (ISIPUB), male and female versions, the Structured Clinical Interview for the diagnosis of DSM-IV sexual disorders, the Female Sexual Function Index, the

International Index of Extended Release ectile Function, the Arizona Sexual Experience Scale, and the Kafka's Sexual Behavior Inventory. The profile of responses of patients with OCD were compared to those of patients with SAD by means of the Student's t test and the chi-square test. Results: Patients with OCD exhibited a history of sexual abuse significantly more frequently than patients with SAD (chi=7.70; df=1, p=0.006). Male patients with OCD had significantly less frequent effective Extended Release ections than male patients with SAD (F=5.86, df=23, p=0.05). The rates of the current use of 5HT reuptake inhibitors (SRI) were not significantly different between the two groups, but patients with OCD had significantly higher rates of past use of Sustained Release Is than patients with SAD (chi=9.39; df=1; p=0.002). The group with SAD had more difficulties to reach orgasm (F=.42; 54; p=0.009) than the group with OCD. Male patients with SAD reported not using contraceptive methods significantly more frequently than male patients with OCD (chi=9.99, df=1, p=0.007). Conclusions: Patients with OCD and patients with SAD exhibit different profiles of sexual behavior.

References:

1. Bodinger L, Hermesh H, Aizenberg D, Valevski A, Marom S, Shiloh R, Gothelf D, Zemishlany Z, Weizman A: Sexual function and behavior in social phobia. J Clin Psychiatry 2002; 63: 874-9.
2. Figueira I, Possidente E, Marques C, Hayes K: Sexual dysfunction: a neglected complication of panic disorder and social phobia. Arch Sex Behav 2001; 30: 369-77.

NR658 Wednesday, May 24, 12:00 PM - 2:00 PM

Bupropion SR Treatment of Veterans With PTSD

Mark D. Fossey, M.D. *University of Oklahoma-Tulsa, Psychiatry, 4502 East 41st Street, Tulsa, OK, 74135*, Robert H. Ebert, M.D.

Educational Objectives:

Recognize the efficacy of bupropion SR in the treatment of avoidance and hyperarousal symptoms but not intrusive symptoms in combat veterans with posttraumatic stress disorder (PTSD) and comorbid depression.

Summary:

Objective: This study examines the utility of bupropion Sustained Release in the treatment of PTSD in combat veterans with comorbid depression. *Methods*: Forty-eight veterans were treated for up to eight weeks with bupropion Sustained Release 100-300 mg daily. Patients were assessed at baseline and termination with the Clinician-Administered PTSD Scale (CAPS-2) and the Hamilton Rating Scale for Depression (HAM-D). Clinical Global Impression-Improvement (CGI-I) was determined at termination. Two-tailed t-tests were used to compare mean baseline scores with those at termination with the last observation carried forward. *Results*: At termination, the mean HAM-D score decreased from 27.2 + 7.2 to 23.5 + 10.0 (p=0.006) and the mean total CAPS-2 score decreased from 77.2 + 25.8 to 67.7 + 33.2 (p=0.0088). Significant reductions were seen in the CAPS-2 avoidance (p= 0.0095) and hyperarousal (p=0.002) subscales but not in the reexperiencing subscale (p=0.51). On the CGI-I scale 10 patients were rated much or very much improved. *Conclusions*: In this veteran PTSD population with moderate to severe depression, bupropion Sustained Release showed modest efficacy in the treatment of both depression and the PTSD symptoms of avoidance and hyperarousal. As in a previous study of bupropion in PTSD veterans with milder depression, our study indicated no improvement in reexperiencing symptoms.

References:

1. Schoenfeld FB, Marmar CR, Neylan TC: Current concepts in pharmacotherapy for posttraumatic stress disorder. Psychiatr Serv 2004; 55:519-531.
2. Carnive JM, Clark RD, Calais LA, Qualls C, Tuason VB: Bupropion treatment in veterans with posttraumatic stress disorder: an open study. J Clin Psychopharmacol 1988; 18:379-383.

NR659 Wednesday, May 24, 12:00 PM - 2:00 PM

Psychometrically-Defined Executive Function Deficits and Academic/Occupational Outcomes in ADHD Adults

Ronna Fried, Ed.D. *Massachusetts General Hospital, 55 Fruit Street, Boston, MA, 02114*, Joseph Biederman, Michael C. Monuteaux, Carter Petty, Alysa E. Doyle, Eric Mick

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that:

The presence of Psychometrically defined EFDs in ADHD subjects was associated with significant functional morbidity beyond that conferred by the diagnosis of ADHD alone.

Summary:

The main aim of this study was to evaluate the impact of psychometrically-defined EFDs on the functional outcomes in a large sample of well-characterized adults with and without ADHD.

Subjects, aged 18 thru 55 with DSM-IV ADHD, were eligible for this study. We assessed domains of cognitive functioning using measures of sustained attention/vigilance, planning and organization, response inhibition, set shifting and categorization, selective attention and visual scanning, verbal and visual learning, and memory.

We defined four groups: controls without EFD (N=122), controls with EFD (N=23), ADHD without EFD (N=147), and ADHD with EFD (N=66). The ADHD+EFD group had significantly lower levels of overall SES, education, and occupation compared to the other three groups. The ADHD+EFD group demonstrated significantly poorer performance on every academic outcome and achievement score assessed relative to the ADHD group. Subjects in the ADHD+EFD group were over two times more likely to have repeated a grade, needed extra help, and been placed in a special class compared with subjects in the ADHD group.

The presence of Psychometrically defined EFDs in ADHD subjects was associated with significant functional morbidity beyond that conferred by the diagnosis of ADHD alone. More efforts are needed to identify cost effective approaches to screen individuals with ADHD for EFDs.

References:

1. Barkley, R. A. (2001). The executive functions and self-regulation: an evolutionary neuropsychological perspective. Neuropsychology Review, 11, 1-29.
2. Biederman, J., Monuteaux, M., Seidman, L., Doyle, A. E., Mick, E., Wilens, T., et al. (2004). Impact of Executive Function Deficits and ADHD on Academic Outcomes in Children. Journal of Consulting and Clinical Psychology, 72, 757-766.

NR660 Wednesday, May 24, 12:00 PM - 2:00 PM

Pregabalin's Efficacy in Achieving Remission in Outpatients With GAD

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Educational Objectives:

This presentation will improve participants' understanding of the treatment efficacy and safety of pregabalin in ambulatory patients with GAD.

Summary:

Objective: Remission is among the most important measures of treatment efficacy in GAD. Eight weeks is the minimum duration of study for clinical trials assessing remission in GAD. In this 8-week, fixed-dose, open-label, lead-in to a 6-month, double-blind, placebo-controlled relapse-prevention study of pregabalin (an α_2-δ ligand) in GAD, we performed a subanalysis to evaluate rates of remission. **Methods:** Outpatients with GAD for ≥1 year received open-label pregabalin (450 mg/day) for 8 weeks. Remission was defined as HAM-A total score ≤7 at LOCF-endpoint. **Results:** Mean age was 37.2 years; 58% of patients were women; and 85% were white. Mean duration of GAD was 11 years. Forty-seven percent and 52% of patients with a baseline HAM-A score >24 and ≤24, respectively, achieved remission of GAD by Week 8. Eighty-two of 624 patients (13.1%) at the fixed dose of 450 mg/day withdrew because of adverse events (AEs). The most common AEs leading to discontinuation were somnolence (3.8%), dizziness (2.7%), and poor concentration (1.8%). **Conclusion:** Pregabalin's promising results from this open-label subanalysis of remission of symptoms in GAD warrant further investigation in a randomized, double-blind, controlled clinical trial. Pregabalin was safe and well tolerated by the majority of GAD patients.

References:

1. Rickels K, Pollack MH, Feltner DE, et al. Pregabalin for treatment of generalized anxiety disorder: a 4-week, multicenter, double-blind, placebo-controlled trial of pregabalin and alprazolam. Arch Gen Psychiatry. 2005;62:1022-1030.
2. Pohl RB, Feltner DE, Fieve RR, Pande AC. Efficacy of pregabalin in the treatment of generalized anxiety disorder: double-blind, placebo-controlled comparison of BID versus TID dosing. J Clin Psychopharmacol. 2005;25:151-158.

NR661 Wednesday, May 24, 12:00 PM - 2:00 PM

Atomoxetine Treatment for Pediatric Patients With ADHD Comorbid Anxiety Disorder

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to summarize the effects of atomoxetine compared to placebo on symptoms and functional outcomes in children with attention-deficit/hyperactivity disorder and comorbid anxiety disorder.

Summary:

Objective: Research suggests that 25-50% of children with ADHD also suffer from anxiety disorders(1). Stimulant treatment of this comorbid subgroup is complicated by potential adverse effects(2). Atomoxetine, a nonstimulant medication approved for treatment of pediatric and adult ADHD, was compared with placebo for treatment of children with ADHD and comorbid anxiety disorders.

Methods: In this double-blind, acute phase of a multicenter study, children meeting DSM-IV criteria for ADHD and either GAD, separation anxiety disorder, or social phobia were randomized to 12 weeks of atomoxetine treatment (n=87) or placebo (n=89). Changes in efficacy and functional outcome scores (from baseline to last observation carried forward endpoint) were compared across treatment groups using analysis of covariance.

Results: Sixty-six patients in each treatment group completed the study (p=ns for any reason for discontinuation). Mean scores improved significantly for atomoxetine versus placebo, respectively, on the Multidimensional Anxiety Scale for Children (-4.6 versus 2.1; p=.009), Life Participation Scale for ADHD-Revised (9.6 versus 2.5; p=.001), and Child Health Questionnaire-Parent-Completed Full Length (6.9 versus 3.3; p=.019).

Conclusion: Results suggest atomoxetine is efficacious and improves functioning in children and adolescents with ADHD and comorbid anxiety disorder.

References:

1. Biederman J, Newcorn J, Sprich S: Comorbidity of attention-deficit/hyperactivity disorder with conduct, depressive, anxiety and other disorders. Am J Psych 1991; 148:564-577.
2. Urman R, Ickowicz A, Fulford P, Tannock R: An exaggerated cardiovascular response to methylphenidate in ADHD children with anxiety. J Child Adolesc Psychopharmacol 1995; 5:29-37.

NR662 Wednesday, May 24, 12:00 PM - 2:00 PM

Open-Label Trial of Atomoxetine in Preschool Children With ADHD

Jaswinder K. Ghuman, M.D. *University of Arizona, Child and Adolescent Psychiatry, 1501 N. campbell Avenue, Tucson, AZ, 85724*, Sophia Vanood, Harinder Singh Ghuman, M.D.

Educational Objectives:

At the conclusion of this presentation, the participants will become familiar with treatment response and side effects of atomoxetine in preschool children with ADHD.

Summary:

Objective: ADHD is an impairing and chronic disorder that often begins in preschool years. Atomoxetine (ATMX) has been found to be helpful in schoolage children with ADHD. We report preliminary data regarding safety and efficacy of ATMX in 3-5-year-old preschool children with ADHD. We hypothesized that ATMX treatment will improve the end of study Swanson, Nolan And Pelham (SNAP) hyperactive/impulsive (HI) subscale scores compared to the baseline scores.

Methods: Six boys and two girls (N=8; mean age=61+9.5 months) diagnosed with ADHD (hyperactive/impulsive type=5 and combined type=3; mean number of DSM IV hyperactive/impulsive symptoms=7.9+0.99 and inattentive symptoms=5.4+1.9; SNAP hyperactive/ impulsive (HI) subscale score=23+2.6; Clinical Global Impression Severity of Illness (CGI-SI) score=5.25+0.71; and Clinical Global Assessment Scale (CGAS) score=50.75+3.96 were enrolled in the open-label ATMX study. Additional children are being recruited.

Each child first participated in a step-wise open-label titration of ATMX to determine his/her "best dose" followed by a 4-week open-label maintenance on the "best dose". ATMX dose was initiated at 0.5 mg/kg/day to a maximium dose of 1.8 mg/kg/day based on therapeutic response and tolerability. Pre-treatment efficacy assessments were conducted at baseline and repeated weekly during titration and every other week during maintenance.

Results: Mean difference in the baseline and end of study visit scores were: SNAP-HI=11.5 (df =7, t=3.26, p=0.0084); CGI-SI= 1.25 (t=3.42, p=0.0112) and CGI-Global Improvement=2.125 (t= 9.379, p<0.0001); and CGAS= -11.375 (t= -3.397, p=0.0115). Adverse events included stomach upset=3, reduced appetite=2, crying/irritable=2, sleepy/tired=2, difficulty sleeping=1, and increased thirst=1. Adverse events were of mild to moderate severity and didn't lead to study drug discontinuation.

Conclusion: Preliminary data analysis of this open-label pilot study shows that ATMX is safe and effective in preschool children with ADHD. Study supported by NIMH-K23-MH01883-01A1.

References:

1. Kratochvil CJ, Vaughan BS, Daughton JM, Mayfield-Jorgensen ML, Burke WJ. Atomoxetine in the treatment of attention deficit hyperactivity disorder. Expert Rev Neurother. 2004 Jul;4(4):601-11.
2. Swanson, J. M. (1992). School-based assessments and interventions for ADD students. Irvine, CA: K. C. Publications.

NR663 Wednesday, May 24, 12:00 PM - 2:00 PM

Recruitment and Retention Issues in Psychopharmacological Research Involving Preschool Children

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Educational Objectives:

At the conclusion of this presentation, the participants will have a better understanding of issues involved in recruiting and retaining preschool children with developmental disorders in psychopharamcological research.

Summary:

Objective: Reports of increased "off-label" prescription of psychopharmacological agents in preschool children are of great public health concern and have lead to a greater emphasis on the importance of well-designed, randomized and controlled psychopharmacological trials involving preschool children. However, preschool psychopharmacological trials face serious challenges in recruiting and retaining research participants. This study examined the efforts needed and obstacles encountered in recruiting preschool children with developmental disorders in a double-blind crossover study to evaluate methylphenidate efficacy and safety for the symptoms of hyperactivity, impulsivity and inattention.

Method: Data from the calls received in response to advertising and outreach efforts regarding the study was examined to explore factors that aided or hindered recruitment. Parents and professionals were informed that we were interested in recruiting 3-6 year old children with a diagnosis of pervasive developmental disorder or mental retardation and symptoms of hyperactivity, impulsivity and inattention. They were informed that eligible children will be seen weekly and participate in a single-blind stepwise methylphenidate titration followed by a 4-week double-blind crossover phase with each child receiving placebo for 2 weeks and child's "best dose" for 2 weeks.

Results: Of the 397 telephone calls received, 163 children were considered potentially eligible for study participation and 10 children completed the entire study protocol. Reasons for attrition included: caregiver not interested in medication for their child= 106/163 (65%) and not able to commit to required weekly appointments or completing rating scales = 40/163 (24.54%). Of the remaining 17 children who participated in screening assessments, 6 children did not meet study eligibility criteria and 1 child couldn't swallow the study capsule.

Conclusion: A major barrier to study participation was parents' reluctance to medicate their preschool child. We will discuss strategies and alternate research designs that do not unduly limit family's treatment options or increase burden of reserach participation.

References:

1. Hinshaw SP et al. (2004). AACAP 2001 research forum: challenges and recommendations regarding recruitment and retention of participants in research investigations. J Am Acad Child Adolesc Psychiatry. 43(8):1037-45.
2. Zito JM, Safer DJ, dosReis S, Gardner JF, Boles M, Lynch F (2000), Trends in the prescribing of psychotropic medications to preschoolers. JAMA 283:1025-1030.

NR664 Wednesday, May 24, 12:00 PM - 2:00 PM

Improved Tolerability Over Time With Mixed Amphetamine Salts Extended Release in Adolescents

Stephen Grcevich, M.D. *The Family Center By the Falls, 8401 Chagrin Road, Ste 14B, Chagrin Falls, OH, 44023*

Educational Objectives:

At the conclusion of this session, participants should be able to:

Describe how some adverse events decrease in frequency in adolescents aged 13 to 17 years with attention-deficit/hyperactivity disorder treated with mixed amphetamine salts extended release (MAS XR) 10-30 mg/d

Recognize the ephemeral experience of adverse events in adolescents treated with MAS XR

Summary:

Introduction: Potential changes in tolerability of psychostimulant treatment over time in adolescents with ADHD are not well characterized.

Methods: Adolescents 13-17 years old with ADHD received placebo (n=69) or mixed amphetamine salts extended release (MAS XR) 10-60 mg/d (n=258) in this 4-week randomized, placebo-controlled, double-blind, parallel-group trial. Six adverse events_anorexia, abdominal pain, headache, emotional lability, insomnia, nervousness_were evaluated for weekly frequency changes. Overall weight loss throughout the trial was also examined.

Results: Overall adverse event frequency decreased from week 1 (MAS XR, 49.2%; placebo, 21.7%) to week 4 (MAS XR, 8.7%; placebo, 4.7%). Few premature discontinuations were due to an AE (MAS XR, 8 of 258 [3.1%]; placebo, 0 of 69 [0%]). Emotional lability, insomnia, and nervousness remained infrequent with placebo (range, 0.0%-2.9%); these adverse events were more common with MAS XR but decreased from week 1 (2.3%, 7.0%, 3.9%, respectively) to week 4 (0.0%, 1.7%, 1.7%, respectively). Abdominal pain and anorexia were also more common with MAS XR, but decreased over time (week 1 [4.3%], week 4 [1.7%] and week 1 [22.1%], week 4 [1.7%], respectively). Headache was similar between the treatment groups and decreased with MAS XR (week 1, 9.7%, week 4, 1.7%) or placebo (week 1, 11.6%, week 4, 4.7%). No placebo subjects reported weight loss as an AE, compared with 26 MAS XR subjects (10.1%). Longer-term follow-up is necessary to determine if reports of weight loss decrease with continued therapy.

Conclusions: In adolescents with ADHD given MAS XR 10-60 mg/d over 4 weeks, AE frequency decreased and only 3.1% of subjects discontinued because of an AE. These results suggest that adolescents who experience AEs during initial MAS XR exposure should be educated about the anticipated improvements in tolerability with continued therapy.

This study was funded by Shire Pharmaceuticals Inc.

References:

1. Greenhill LL, et al. Practice parameter for the use of stimulant medications in the treatment of children, adolescents, and adults. J Am Acad Child Adolesc Psychiatry. 2002;41(2 Suppl):26S-49S.
2. Spencer TJ, et al. Efficacy and safety of mixed amphetamine salts extended release (Adderall XR) in the management of attention-deficit/hyperactivity disorder in adolescent patients.Clin Ther. 2005. In Press.

NR665 Wednesday, May 24, 12:00 PM - 2:00 PM

Early Predictors of Later PTSD and Depression in Battle-Injured Soldiers

Thomas A. Grieger, M.D. *Uniformed Services University, B-3068, USUHS, 4301 Jones Bridge Road, Bethesda, MD, 20814*, Stephen J. Cozza, M.D., David M. Benedek, M.D., Charles C. Engel, M.D., Patricia Martinez, B.S.N., Harold J. Wain, Ph.D., Robert J. Ursano, M.D.

Educational Objectives:

At the conclusion of this presentation participants should be able to:

1. Discuss pain during hospitalization as a risk factor for later PTSD and depression
2. Describe the changing reates of psychiatric illness among battle injured soldiers accross time

Summary:

Introduction/Hypothesis: Prior study of soldiers injured in combat in Afghanistan and Iraq showed increasing rates of probable PTSD and depression following discharge from hospital. This study examines early predictors of later PTSD and depression among 294 seriously injured soldiers following post-injury hospitalization. **Methods:** In this cohort analytic study, consecutive soldiers (N=294) evacuated for combat injuries completed a battery of standardized screening instruments during hospitalization (one month after injury) and at six-month follow-up. A 7-item pain scale derived from the Patient Health Questionnaire (PHQ-15) was used to assess pain during initial hospitalization. Patients scoring in the upper quartile on this measure were compared with those scoring lower levels of pain. Probable PTSD was assessed using the PTSD Checklist; probable depression was assessed using the Patient Health Questionnaire (PHQ-9). Statistical analysis was performed using binary logistic regression with multiple variable entries. **Results**: At initial evaluation 4% of soldiers met criteria for PTSD and 4% met criteria for depression. At 6 month follow up 12% met criteria for PTSD and 9% met criteria for depression. After controlling for demographic characteristics and presence of PTSD or depression during initial hospitalization, high levels of pain reported during hospitalization resulted in a 5 times greater risk for PTSD and 3.4 times greater risk for depression at 6 month follow up. **Conclusions**: Screening of battle-injured soldiers for PTSD and depression during initial hospitalization did not accurately identify those who had these disorders at 6 month follow up. Greater endorsement of pain during hospitalization was predictive of later PTSD and depression even after controlling for initial presence of these disorders. Careful assessment of post-injury pain may be a valuable tool to identify those at higher risk for later developing psychiatric disorders following trauma.

References:

1. O'Donnell ML, Creamer M, Pattison P, et al: Psychiatric morbidity following injury, American Journal of Psychiatry 161:507-514, 2004.
2. Grieger TA, Waldrep DA, Movasz MM, and Ursano RJ: Follow-up of Pentagon employees two years after the terrorsit attack of September 11, 2001, Psychiatric Services 56:1374-1378, 2005.

NR666 Wednesday, May 24, 12:00 PM - 2:00 PM

Psychosocial and Psychiatric Morbidity in Indian Patients Suffering With Acne

Surendra Kumar Mattoo, M.D. *Chandigarh, India*, Sanjeev Handa, M.D., Nitin Gupta, M.D., Nitasha Khera, M.A., Shveta Dogra, M.A.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to [1] demonstrate the relevance of cross-cultural research in psychological/psychiatric issues related to dermatological disorders, and [2] highlight the importance of identifying and managing psychiatric and psychosocial morbidity in acne.

Summary:

Objective: Acne, a common dermatological disorder, is well known to be associated with psychological morbidity. However, the database on this aspect from the developing countries (especially India) is limited. This study was carried out to determine the prevalence of psychosocial and psychiatric morbidity in patients with acne.

Methods: In this prospective cross-sectional study, outpatients with acne (N=50) were studied, with an age and education matched healthy control (N=55) group. Additionally two subgroups of acne, based on General Health Questionnaire-12 (GHQ) cut-off score of >2, were generated i.e. GHQ positive (N=13) and GHQ negative (N=37). These two sub-groups were compared as regards psychiatric morbidity (Comprehensive Psychopathological Rating Scale [CPRS]) and psychosocial variables of quality of life, coping and dysfunction.

Results: Psychiatric morbidity as per GHQ-12 was identified in 13 subjects (prevalence rate of 26%). As per International Classification of Diseases-Tenth Revision (ICD-10) diagnosis, Adjustment disorder- depressive type or Depressive episode were found in the GHQ positive sub-group. On comparison, GHQ positive sub-group was characterised by-more unmarried males, longer duration of illness, poorer QOL, and more frequent use of coping strategies.

Conclusion: There is a high prevalence rate of psychosocial morbidity in patients with acne, who suffer froma poor QOL. This study highlights the need to develop a cross-cultural database on psychosocial aspects and psychiatric morbidity associated with acne.

Funding: This study was carried out as part of the Institute (PGIMER) Research Scheme entitled "Coping and quality of life in air borne contact dermatitis" and was supported by funding provided by the Institute-Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, India.

References:

1. Picardi A, Abeni D, Melchi CF, Puddu P, Pasquini P: Psychiatric morbidity in dermatological outpatients: an issue to be recognised. Br J Dermatol 2000; 143(5): 983-91.
2. Baldwin HE: The interaction between acne vulgaris and the psyche. Cutis 2002; 70(2): 133-9.

NR667 Wednesday, May 24, 12:00 PM - 2:00 PM

Subthreshold PTSD and Related Factors Following Marmara Earthquake in Turkey

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to demonstrate that DSM-IV diagnostic criteria for PTSD should be reviewed.

Summary:

Introduction: PTSD diagnosis criteria may be highly restrictive in DSM-IV. Some trauma victims may have symptoms although they do not meet the DSM criteria. Some authors have suggested the diagnoses *partial PTSD and subthreshold PTSD* (1,2). Results of previous research have led to dispute whether subthreshold

PTSD is a clinical diagnosis or not (2). We hypothesized that no differences exist in quality of life, disability, and psychiatric comorbidity between subthreshold PTSD and PTSD and suggest that the three avoidance criteria for PTSD diagnosis be reduced to two.

Methods: The study group was composed of people present at the Marmara earthquake in 1999. People who took part in the study were given the Composite International Diagnostic Interview, Clinician Administered PTSD Scale, Short Form-36, Brief Disability Scale, and the Beck Depression Inventory. The subthreshold PTSD group was defined according to CAPS results for PTSD diagnosis using two instead of three group-C avoidance criteria.

Results: The study group consisted of 77 women and 35 men (mean age, 37.9 ± 13.3 years). Four subgroups included PTSD (n = 25), subthreshold-PTSD (n = 29), healthy subjects who survived a major trauma (n = 36), and healthy subjects who did not survive a major trauma (n = 22). People with subthreshold PTSD who survived the earthquake had the same quality of life points compared with people with PTSD. Quality of life points and disability were higher for persons in the subthreshold PTSD group than they were for healthy subjects who did not survive a major trauma.

Conclusions: The results of the current research demonstrate that a subthreshold PTSD group exists, which was different from chronic PTSD in terms of disability and psychiatric comorbidity. However, in agreement with previous research, the current study points to the fact that DSM-IV diagnostic criteria for PTSD should be reviewed.

References:

1. 1. Carlier IVE, Gersons BPR: Partial posttraumatic stress disorder (PTSD): the issue of psychological scars and the occurance of PTSD symptoms. Journal of Nervous and Mental Disorders 1995; 183:107-109.
2. 2. Zlotnick C, Franklin CL, Zimmerman M : Does.

NR668 Wednesday, May 24, 12:00 PM - 2:00 PM

Characterizing Anxiety Disorders in Children and Adolescents With ADHD

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Educational Objectives:

At the conclusion of this presentation, the participant should recognize the presence of pediatric anxiety disorders in the presence of ADHD, as well as in youth without ADHD. The participant should demonstrate knowledge regarding the full complement of pediatric anxiety disorders.

Summary:

Objective The aim of this study was to evaluate moderating effects of pediatric ADHD and Anxiety disorders on each other. *Methods* Data was analyzed from a large clinical sample of children with ADHD (n=509), Anxiety disorders (n=251), and comorbid ADHD+Anxiety (n=704). Subjects were referred to a pediatric psychopharmacology program at a major academic center. Diagnoses were obtained by Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS-E). *Results* Comparisons between groups controlled for baseline differences in gender and social-economic scores. Overall, rates of Anxiety disorders were not significantly different in children with or without ADHD. However, greater rates of Panic disorder (19% versus 9%), and Obsessive Compulsive Disorder (27% versus 15%) were observed in the Anxiety group, compared to the other groups. Greater rates of Bipolar disorder were observed in the ADHD+Anxiety group compared to the other groups (27% versus 13%). Greater rates of Major Depression were observed in the Anxiety group (66%) and ADHD+Anxiety group (63%), compared to the ADHD group (33%). Rates of Oppositional Defiant Disorder were greater in the ADHD groups (54-67%) compared to the Anxiety group (41%). Similar findings were observed for Conduct Disorder. High rates of educational impairment were observed in all groups. Global assessment of functioning ratings were comparably low among groups. *Conclusions* Overall, the rate of Anxiety disorders was not significantly different in children with or without ADHD. However, higher rates of Panic, OCD and comorbid Depression were observed in children with Anxiety, higher rates of Bipolar disorder in the comorbid ADHD+Anxiety group, and higher rates of comorbid disruptive disorders in children with ADHD, with or without anxiety. Future analysis will examine putative bidirectional moderating effects; the impact of Anxiety disorders on ADHD symptomatology.

References:

1. Perrin S, Last CG: Relationship between ADHD and anxiety in boys: results from a family study. J Am Acad Child Adolesc Psychiatry 1996; 35(8):988-96.
2. Neuman RJ, Heath A, Reich W, Bucholz KK, Madden PAF, Sun L, Todd RD, Hudziak JJ: Latent class analysis of ADHD and comorbid symptoms in a population sample of adolescent female twins. J Child Psychol Psychiatry 2001; 42(7):933-42.

NR669 Wednesday, May 24, 12:00 PM - 2:00 PM

Imagination of Fearful Scenarios Induces Hyperventilation and Subjective Symptoms in Patients With Medically Unexplained

Jiangna Han, M.D. *PUMC hospital, Pneumology, Department of Pneumology, Peking Union Medical College Hospital, Beijing, 100730, China*, Yuanjue Zhu, M.D., Shunwei Li, M.D., Dongmei Luo, R.N., *Ilse Van Diest, Ph.D., *Omer Van den Bergh, Ph.D., **Karel P. Van de Woestijne, M.D.

Educational Objectives:

At the conclusion of this presentation, the participants should be able to learn the impact of anxiety on breathing control system and the role of hyperventilation in the development of subjective symptoms in patients with so-called medically unexplained dyspnea.

Summary:

Study objectives: The concept "medically unexplained dyspnea" refers to a group of difficult patients who present with marked dyspnea without any disability that might explain the symptoms. Their dyspnea is usually associated with enhanced fear and anxiety. We investigated the role of imagined fear in provoking subjective symptoms, specifically dyspnea, in those patients.

Measurements: Forty patients with medically unexplained dyspnea and 40 matched normal subjects were exposed to scripts and asked to imagine both fearful and restful scenarios, while end-tidal PCO_2 ($PetCO_2$) and breathing frequency were recorded and subjective symptoms evaluated.

Results: Imagination of fearful scenarios (being blocked in an elevator, in particular) induced anxious feelings and elicited a significant fall of $PetCO_2$ in the patients. Breathing frequency increased accordingly. Symptoms of dyspnea, palpitation or fast heart beat, and paraesthesias increased. These induced subjective symptoms correlated with the fall of $PetCO_2$.

Conclusions: Imagination of fearful scenarios induces hyperventilation and provokes subjective symptoms in the patients with medically unexplained dyspnea.

This research was supported by grant BIL01/05 of the Bilateral Scientific and Technological Cooperation between China and Belgium (Flanders).

References:

1. Han JN, Stegen K, Simkens K, Cauberghs M, Schepers R, Van den Bergh O, Clement J, Van de Woestijne KP: Unsteadiness of breathing in patients with hyperventilation syndrome and anxiety disorders. Eur Respir J 1997; 10:167-76.
2. Van Diest I, Winters W, Devriese S, Vercamst E, Han JN, Van de Woestijne KP, Van den Bergh O: Hyperventilation beyong fight/flight: respiratory responses during emotional imagery. Psychophysiology 2001; 38:961-968.

NR670 Wednesday, May 24, 12:00 PM - 2:00 PM

Preschool Behavioral Disinhibition Predisposes to Comorbid Mood and Disruptive Behavior Disorders

Dina R. Hirshfeld-Becker, Ph.D. *Mass General Hospital, Pediatric Psychopharmacology, 185 Alewife Brook Pkwy, Suite 2100, Cambridge, MA, 02138*, Joseph Biederman, M.D., Aude I. Henin, Ph.D., Bonnie Kaufman, B.A., Sophie De Figueiredo, Ph.D., Jerrold F. Rosenbaum

Educational Objectives:

1. At the conclusion of this poster presentation, the participant should understand the definition of temperamental behavioral disinhibition and how it can be assessed through laboratory observations.
2. At the conclusion of this poster presentation, the participant should know about new data on the clinical outcomes of preschool behavioral disinhibition in middle childhood.
3. At the conclusion of this poster presentation, the participant should understand the clinical and scientific implications of these new longitudinal data.

Summary:

Objective: Behavioral disinhibition represents the temperamental tendency to respond to novel situations with increased exploratory behavior and disinhibition of speech and action. The purpose of this study was to test the hypothesis that behavioral disinhibition is a risk factor for disruptive behavior and comorbid mood disorders. Methods: In this longitudinal study of offspring of parents with panic disorder and depression (N=284), we assessed behavioral disinhibition and inhibition using one age-specific standardized laboratory observation at baseline, when children were between the ages of 2 and 6 years. At 5-year follow-up, we assessed psychiatric outcomes in 216 (76%) of the children using the Schedule for Affective Disorders and Schizophrenie (Kiddie-SADS-E). Results: Compared with children who were neither disinhibited or inhibited (N=73), behaviorally disinhibited children (N=75) had significantly higher lifetime rates of comorbid mood and disruptive behavior disorders (15% versus 1% in disinhibited versus others, Odds Ratio=12.38, p<.01). They also had significantly higher current rates of any disruptive behavior disorder (29% versus 10%, Odds Ratio=3.91, p<.01), oppositional defiant disorder (23% versus 5%, Odds Ratio=5.06, p<.01), and comorbid mood and disruptive behavior disorders (7% versus 0%, p=.031 by Fisherâ€™s exact test. Conclusions: This study provides prospective evidence that behavioral disinhibition observed at ages 2-6 years represents a prospective risk factor for behavioral and affective dysregulation in middle childhood. Results suggest that behaviorally disinhibited children should be monitored clinically for onset of disruptive behavior and mood disorders and may benefit from early intervention.

References:

1. Hirshfeld-Becker DR, Biederman J, Faraone SV, Violette H, Wrightsman J, Rosenbaum JF: Temperamental correlates of disruptive behavior disorders in young children: preliminary findings. Biological Psychiatry 2002; 50:563-574.
2. Hirshfeld-Becker DR, Biederman J, Calltharp S, Rosenbaum ED, Rosenbaum JF. Behavioral inhibition and disinhibition as hypothesized precursors to psychopathology: Implications for pediatric bipolar disorder. Biological Psychiatry 2003; 53: 985-99.

NR671 Wednesday, May 24, 12:00 PM - 2:00 PM

Investigation of Familial Pediatric Bipolar Disorder I, II, or NOS

Meghan E. Howe, M.S.W. *Stanford University, Department of Child and Adolescent Psychiatry, 401 Quarry Rd, Stanford, CA, 94304*, Kim Gallelli, Ph.D., Jess Yee, Kiki Chang, M.D.

Educational Objectives:

1. Participants will learn about the spectrum of pediatric bipolar disorder in offspring of parents with bipolar.

Summary:

Objective: We sought to study a cohort of children with bipolar disorder (BD) who are offspring of parents with BD in order to examine the possible similarities and differences among bipolar disorder type I, II, and NOS.

Method: 93 families with at least one bipolar parent (mean age = 41.8, 76.3% female) were interviewed for family history and diagnosis using the FH-RDC and SCID respectively. Additionally, all children (n= 93; mean age = 12.9, Â±3.4) were assessed using the WASH-U-KSADS. During the interview comprehensive medication history and number of psychiatric hospitalizations was gleaned, and CGAS score assigned. Additionally, manic and depressive symptoms were captured on the YMRS and CDRS-R. BD type I and II were defined by DSM-IV criteria. BD NOS was defined as a mood episode of euphoric, elevated, or expansive mood plus 2 symptoms or irritable mood plus 3 symptoms that caused impairment in functioning for 2 to 3 days.

Results: 52 children were diagnosed with BD I, 16 with BD II, and 25 with BD NOS. Regardless of BD type, children with BD who are offspring of adults with BD have similar rates of family history of mood disorders (p= .42), and duration of medication exposure (p=.41). Children with BD I, II, or NOS all had similar cgas (p=.46), ymrs (p= .32), and cdrs-r (p=.44) scores. However, children diagnosed with BD II and BD NOS tended (p =.06) to be exposed to more different types of mood stabilizers and antipsychotic medications.

Conclusions: The results of this analysis suggest that familial pediatric bipolar disorder is similar in presentation and impairment regardless of diagnostic type of bipolar. Furthermore, children with a diagnosis of BD NOS may be exhibiting subsyndromal symptoms of bipolar disorder type I or II.

References:

1. Chang, KD, Steiner, H, Ketter, TA (2003): Studies of offspring of parents with bipolar disorder. Am J Medical Genetics 123C:26-35.
2. Chang, KD, Steiner, H, Dienes, K, Adleman, N, Ketter, TA (2003): Bipolar Offspring: A window into bipolar disorder evolution. Biological Psychiatry 53:945-951.

NR672 Wednesday, May 24, 12:00 PM - 2:00 PM

Comparison of Bupropion and Paroxetine in the Treatment of MDD Associated with ADHD

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Educational Objectives:

At the conclusion of this presentation, the participant should have an awareness that the presence of co-morbid mood symptmos with ADHD is not uncommon and be able to identify treatment options for such patients informed by this awareness.

Summary:

Background

There is increasing awareness of co-morbid depressive symptoms occurring with inattentive and hyperactive-impulsive symptoms. Few studies have examined this particular clinical presentation despite ADHD and depression being common comorbidities in youth. Children with ADHD and depression display more impairment in social and academic functioning compared to controls.

Objective

To compare the clinical response of patients with co-morbid ADHD and MDD to bupropion and paroxetine.

Method

This was a three-month open label trial comparing bupropion and paroxetine treatment in patients with MDD and ADHD. Other co-morbidities included Oppositional Defiant Disorder and Conduct Disorder.

Total number of patients was 30 (M=19, F=11). Age range was from 7 to 12 years (average=9.3 years). Patients were randomized to either bupropion or paroxetine. Dosage range of bupropion used was 100 to 150 mg (average= 143. 3 mg) per day. Dosage range of paroxetine used was 10 to 20 mg (average dose= 18 mg). All patients continued treatment of ADHD with methylphenidate for the study duration (either 40 or 60 mg of methylphenidate). The patients were evaluated at baseline, 2 weeks, 4 weeks, 8 weeks and 12 weeks with a Global Assessment of Functioning Score and a 17-item scale which assessed symptoms of ADHD, disruptive behavior and depressive symptoms.

Results

11 patients on bupropion and 6 patients on paroxetine showed significant improvement on the 17 item scale. 2 patients randomized to bupropion and 4 patients randomized to paroxetine showed moderate improvement on the same scale. The group of patients randomized to bupropion showed a more significant improvement in symptoms of hyperactivity as compared to the group randomized to paroxetine.

Conclusions

Depressive symptoms associated with ADHD respond better to bupropion as compared to paroxetine. It may be hypothesized that this difference is related to the impact of bupropion on noradrenergic and dopaminergic pathways.

References:

1. Blackman GL, Ostrander R, Herman KC., Children with ADHD and depression: a multisource, multimethod assessment of clinical, social, and academic functioning, J Atten Disord. 2005 May;8(4):195-207.

2. Manas-Lammers LA. The challenge of childhood depression and ADHD. JAAPA. 2002 Dec;15(12):31-4, 39-40, 56.

NR673 Wednesday, May 24, 12:00 PM - 2:00 PM

Decreased Levels of Soluble P-selectin and L-selectin in Patients with Autistic Disorder

Yasuhide Iwata, M.D. *Hamamatsu University School of Medicine, Psychiatry and Neurology, 1-20-1 Handayama, Hamamatsu, Shizuoka, 431-3192, Japan*, Katsuaki Suzuki, M.D., Masayoshi Kawai, M.D., Koichi Osonoe, M.D., Naoki Kondo, M.D., Katsuhisa Ando, M.D., Norio Mori, Prof. Dr.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that patients with autistic disorder represent immune system dysfunction, and may be involved in the pathogenesis of the illness.

Summary:

Objective: Numerous studies have linked autistic disorder with altered immune function. The selectin family of adhesion molecules plays a prominent role in immune/inflammatory responses. To further study the immunological processes in the pathophysiology of autistic disorder, we determined the serum levels of selectins in patients with autistic disorder.

Method: We studied 19 unmedicated male patients with autistic disorder and age matched 19 healthy male subjects. The serum levels of the three types of soluble-form selectin (sE-, sL-, and sP-selectin) were determined by enzyme-linked immunosorbent assay (ELISA).

Results: Serum levels of sP-selectin and sL-selectin were significantly decreased in patients with schizophrenia compared to those of control subjects ($p < 0.001$ and $p = 0.014$). No significant difference was found with regard to the level of serum sE-selectin.

Conclusion: A decrease in the levels of serum sP-selectin and sL-selectin in patients with autistic disorder may represent immune system dysfunction, and may be involved in the pathogenesis of the illness.

References:

1. Licinio J, Alvarado I, Wong ML: Autoimmunity in autism. Mol Psychiatry 2002; 7:329.

2. Jyonouchi H, Sun S, Le H: Proinflammatory and regulatory cytokine production associated with innate and adaptive imimmune and developmental regression. J Neuroimmunol 2001; 120:170'179.

NR674 Wednesday, May 24, 12:00 PM - 2:00 PM

A Study on the Polymorphism of COMT Met/Val and Cognitive Function in Han Chinese Children With Tourette's Syndrome

Weidong Ji, Sr., Prof. Dr. *Wuxi Mental Health Center, Qianong road No.156,Wuxi Mental Health Center, Wuxi, 214000, China*

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the important of searching endophenotype for mental disorders.

Summary:

Objective Tourette's syndrome (TS) is a childhood-onset neuro-psychiatric disorder characterised by multiple motor and vocal tics lasting more than one year. In this paper, COMTmet/val gene polymorphism and cognitive function are studied in Children with Tourette's Syndrome.

Method 1.In the present study, we genotyped a large multiplex sample of GTS affected children for polymorphisms in COMT met/val gene. Associations were tested by the transmission disequilibrium test (TDT). 2. 86 Han Chinese children with GTS were tested using a set of neuropsychological test and compared with 51 healthy control group to understand the relationship between cognitive deficits and genetics.

Result 1. Compared with normal children, The GTS group showed impairment on almost all psychological measures. In some stroop test, combined ADHD group differed from the GTS-alone group.2. Subjects with the met/met COMT genotype made significantly fewer perseverative Extended Release rors on the Wisconsin Card Sorting Test than did subjects with the val/val genotype. The individual carried COMT met allele differed from individuals carried

COMT val allele in delayed memory, WCST Extended Release rors and perseverative Extended Release rors.

Conclusion 1. These data are consistent with the results of other studies examining the role of COMT in cognitive function. GTS subjects with the met allele produced fewer perseverative Extended Release rors on the Wisconsin Card Sorting Test than subjects with the val allele, suggesting that a functional genetic polymorphism may influence prefrontal cognition..

Key words Tourette's syndrome catechol-O-methyltransferase polymorphism cognitive function

References:

1. Akil M, Bhaskar S. Kolachana, et al. Catechol-O-Methyltransferase Genotype and Dopamine Regulation in the Human Brain.The Journal of Neuroscience 2003; 23(6):2008-2013.

2. Rosa A, Zarzuela A, Cuesta M,et al. New evidence for association between COMT gene and prefrontal neurocognitive functions in schizophrenia. Schizophr Res [Suppl] 2002;53:69.

NR675 Wednesday, May 24, 12:00 PM - 2:00 PM

The Inpatient Dilemma: Patients With Mental Retardation and Co-Occuring Mental Illness

Javed Joy, M.D. *Temple U School of Medicine, 100 E Lehigh Ave, Suite 305, MAB, Philadelphia, PA, 19125,* Joseph M. Garbely, D.O., Mark Deskovitz, M.S.

Educational Objectives:

At the conclusion of this poster presentation the participants should be able to:

1. Recognize the unique challenges the psychiatrist encounters when treating patients with mental retartation and co-occuring mental illness.
2. Create a more appropriate treatment milieu on an inpatient unit.
3. Construct a more effcient treatment team approach inculcating behavioral treatment plans and involving outpatient providers in treatment and disposition planning.
4. Improve accuracy of axis I diagnosis.
5. Reduce the incidence of inappropriate psychopharmacology.
6. Understand the role of psychometric testing in guiding diagnostic accuracy and treatment protocols.
7. Decrease recidivism rates.

Summary:

Introduction: 27%-71% of patients with Mental Retardation (MR) have co-occurring mental illness. There is limited research on successful treatment programs, sparse outcome data and a lack of validated psychometric testing in this group. Typically, the clinical focus is on medication to suppress disturbing behavior. Often, these patients have an insufficient length of stay (LOS) necessary to address their complex problems, receive inappropriate medications to treat behavior leading to misdiagnosis in an effort to support medication choice. This disconnect between behavior, treatment and diagnosis led to the necessity of establishing a specialized inpatient unit with the partnership of Philadelphia MR Services.

Methods: Phase I included training new staff; Phase II included developing specialized programming, improving communication with outpatient providers, and optimizing coordination of care; Phase III introduced a battery of psychometric tests designed to improve accuracy of diagnosis and assess degree of functioning; Phase IV was a chart review of the first 100 patients admitted beginning in 2003 with a diagnosis of MR and mental illness.

Results: Pilot data comparing this specialized unit with matched controls in the non-specialized units shows significantly longer LOS (19 days versus 11 days, $p < 0.05$), more definitive diagnoses (e.g. fewer Psychosis NOS diagnoses 0.0% versus 7.3%), and an overall trend towards reduction in the number of medications.

Discussion: Improved diagnostic accuracy, achieved through intensive evaluation permitted by longer LOS, led to appropriate treatment choices and reduction of unnecessary medications and side effects. Ongoing prospective data measuring congruence between behavior, diagnosis and treatment, medication side effects, recidivism, and impact of psychometrics including our modified PANSS on diagnostic accuracy will be analyzed and presented. This research has the potential to redefine diagnostic approaches, treatment strategies, and quality of care in this challenging yet ever-rewarding patient population.

References:

1. Cowley A, Newton J, Sturmey P, Boras N, Holt G: Psychiatric Inpatient Admissions of Adults With Intellectual Disabilities: Predictive Factors. American Journal on Mental Retardation 2005; 110, No. 3: 216-225.

2. Moss S, Emerson E, Kiernan C, Turner S, Hatton C, et al: Psychiatric symptoms in adults with learning disability and challenging behavior. The British Journal of Psychiatry 2000; 177: 452-456.

NR676 Wednesday, May 24, 12:00 PM - 2:00 PM

Treatment Effect of Aripiprazole in ADHD With Tourette Disorder: Case Report

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Educational Objectives:

Aripiprazole(Abilify) is an atypical antipsychotic with dopamine partial agonistic characteristics.

It is known that ADHD is cause by a decrease of dopamine in the frontal lobe, and that ADHD is usually accompanied by tic disorders or Tourette disorders. Anti-dopaminergic drug can often lead to an improvement of symptoms caused by Tourette disorder.

We would like to report and consider a scenario that is very common in the clinical setting, but not supported by theory. We injected 15 mg of the dopamine partial agonistic, Aripipzazole which lead to an obvious improvement of symptoms in patients with Tourette disorders.

Summary:

An 8-year-old boy, presenting with ADHD and Tourette disorders. The patient was on 2 mg of rispedal for 4 months, but there was little improvement and the symptoms of ADHD progressed. With the consent of the parents, the patient stopped rispedal treatments and started 15mg of aripiprazole. Using the Yale Tic Disorders test and ACRS and visual and auditory ADS for ADHD severity check. CDI, K-PIC scale and CBCL scale for patient's psychiatric status. On the tic symptom after giving 15mg of Aripiprazole a child scored 15 on vocal tic, 14 on motor tic and he showed no progress on the level of tic disorder and over all impression. His score of vocal tic and motor tic on self-report, vocal tic score was 9 and motor tic score was 10. A score of 17 on ACRS was noted with 71/91(converted score) points for Omission/Commission on the visual TOVA, and 52/81 points on the auditory TOVA. After 1month using Aripiprazole, A score of 108/104 on Ommission/Commission on the visual TOVA, and a score of 70/86 on the auditory TOVA. According to the parents observation, after changing to Aripiprazole injections, the patients aggressiveness diminished and peer to peer relationship was improved. This represented a worsening state. In the interview and examination taken after 1 month of 15mg of Aripiprazole, the level of severity was reduced, minor level of sufferings, and the slight progress

of overall impression. Although the patent still showed violent behaviors like temper tantrum overall school life showed improvement. The patient who has both Tourette disorders and ADHD, showed temporarily worsening of ADHD symptoms after treatments with 15mg of Aripiprazole, however Tic Disorders and aggressiveness improved a little. As time goes by, some improvements were observed in ADHD symptoms.

References:

1. Lieberman JA. Dopamine partial agonists: a new class of antipsychotic.
2. Berardelli A, Curra A, Fabbrini G, Gilio F, Manfredi M. Pathophysiology of tics and Tourette syndrome. J Neurol. 2003 Jul;250(7):781-7.

NR677 Wednesday, May 24, 12:00 PM - 2:00 PM

A New Community Based Approach to the Care of the Chronically Ill Eating Disorder Client: An Assertive Community Treatment Program for Eating Disorders (ED ACT)

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to:

1) identify the treatment goals, the target population and treatment modalities for an ED ACT program

2) describe the demographic and clinical characteristics of the cohort who are treated in an ED ACT program

3) identify the psychometric instruments needed for program evaluation and the recognize the importance of evaluating outcome

Summary:

The model of care of ACT, which provides client centered, community based intervention for clients with serious and persistent mental illness, has been widely adopted across North America, especially for clients with psychotic illness. This model has recently been adapted for clients with serious chronic and disabling eating disorders (ED), for whom there are few if any effective evidence based treatments available. This new ED ACT program has been operating since April 2005. The goals of this new program are to improve the quality of life of psychosocially disabled and medically unstable ED clients and to reduce their rates of recidivism and rehospitalization. The conceptualization and implementation of this program will be described as well as one year outcome data. The disposition of the first 22 clients with ED who have been referred to the program will be presented. Current active clients all have anorexia nervosa, have a mean age 33.6 (7.1) years, are mainly single (86%), are predominately of the restricting subtype (71%) with a mean duration of illness 16.2 (6.6) years and a mean current BMI 17.1 (1.8). They have a mean BDI score of 31.0 (17.2) and a mean BAI score of 29.0 (10.3) at entry into the program. In conclusion, this innovative model of care is applicable to seriously ill clients with ED and can be taught to staff and implemented in the community. Further research will determine if the model is effective in reducing morbidity and mortality of individuals with chronic ED.

References:

1. Dixon L: Assertive Community Treatment: Twenty-Five Years of Gold. Psychiatric Services 2000; 51:759-765.
2. Kaplan AS and Garfinkel PE: Difficulties in Treating Patients with Eating Disorders: A Review of Patient and Clinican Variables. Canadian Journal of Psychiatry 1999; 44: 665-670.

NR678 Wednesday, May 24, 12:00 PM - 2:00 PM

Effect of Mixed Amphetamine Salts Extended Release on Neurocognitive Speed in Young Adults With ADHD

Gary Kay, Ph.D. *Washington Neuropsych Institute, 4910 Massachusetts Avenue NW, Suite 100, Washington, DC, 20016*

Educational Objectives:

At the conclusion of this session, participants should be able to describe the improvements in neurocognitive speed in young adults with attention-deficit/hyperactivity disorder treated with mixed amphetamine salts extended release 20-50 mg/d and recognize the relative benefits of performing neurocognitive tasks while receiving stimulant therapy.

Summary:

Introduction: Stimulant treatment for ADHD has shown increased reaction time during neurocognitive tasks. Neurocognitive speed was evaluated in young adults receiving mixed amphetamine salts extended release (MAS XR) for ADHD.

Methods: This 6-week, randomized, single-center, double-blind, placebo-controlled, 2-way crossover study evaluated the effect of MAS XR 20-50 mg/d or placebo on neurocognitive functioning in adults aged 19-25 years with ADHD. All subjects received active treatment and placebo for 3 weeks. Improvement in speed was measured using Symbol Digit Coding, Divided Attention Test (Dual) Sequence Comparison, Matching to Sample, and Pathfinder (Number and Combined [Number+Letter]). Data were evaluated by ANCOVA with education as a covariate and alpha=.05.

Results: Fifteen adults comprised the intent-to-treat population. All subjects were included in the MAS XR and placebo groups. Results in order of study drug administration were: MAS XR first= MAS XR for 3 weeks, then placebo for 3 weeks; Placebo first= placebo for 3 weeks, then MAS XR for 3 weeks. Results for speed were 1) Symbol Digit Coding-MAS XR first: MAS XR=49.25, placebo=52.15, Placebo first: placebo=43.90, MAS XR=47.96 ($F=5.607$; $p=.037$); 2) Divided Attention Test-MAS XR first: MAS XR= 31.81, placebo=33.62, Placebo first: placebo=34.61, MAS XR= 40.11 ($F=9.260$; $p=.011$); 3) Matching to Sample-MAS XR first: MAS XR=56.34, placebo=54.99, Placebo first: placebo=49.05, MAS XR=57.33 ($F=5.778$; $p=.035$); 4) Pathfinder Number-MAS XR first: MAS XR=98.25, placebo=101.98, Placebo first: placebo= 95.67, MAS XR=106.64 ($F=7.027$; $p=.023$); and 5) Pathfinder Combined-MAS XR first: MAS XR=74.14, placebo=82.36, Placebo first: placebo=64.27, MAS XR=77.21 ($F=16.835$; $p=.002$).

Conclusions: Statistically significant improvements on performance time were observed when subjects switched from placebo to MAS XR. A practice effect was observed on most measures: Reaction time continued to improve in subjects even after switching to placebo. Psychostimulant therapy has a neurocognitive advantage in young adults with ADHD.

This study was funded by Shire Pharmaceuticals Inc.

References:

1. Carlson CL. A divided attention analysis of the effects of methylphenidate on the arithmetic performance of children with attention-deficit hyperactivity disorder. J Child Psychol Psychiatry. 1991;32:463-471.
2. Schoechlin C, Engel RR. Neuropsychological performance in adult attention-deficit hyperactivity disorder: meta-analysis of empirical data. Arch Clin Neuropsychol. 2005;20:727-744.

NR679 Wednesday, May 24, 12:00 PM - 2:00 PM

Effect of Mixed Amphetamine Salts Extended Release on Accuracy During Neurocognitive Testing in Young Adults With ADHD

Gary Kay, Ph.D. *Washington Neuropsych Institute, 4910 Massachusetts Avenue NW, Suite 100, Washington, DC, 20016*

Educational Objectives:

At the conclusion of this session, participants should be able to:
- Describe the improvements in neurocognitive function in young adults with attention-deficit/hyperactivity disorder treated with mixed amphetamine salts extended release 20-50 mg/d
- Recognize the relative benefits of performing neurocognitive tasks while receiving stimulant therapy

Summary:

Introduction: Neuropsychological measures of accuracy may help establish the cognitive phenotype of ADHD.

Methods: 6-week, randomized, single-center, double-blind, placebo-controlled, 2-way crossover study evaluating effect of mixed amphetamine salts extended release (MAS XR) 20-50 mg/d or placebo on neurocognitive functioning of adults aged 19-25 years with ADHD. All subjects received active treatment and placebo for 3 weeks. Attention improvement was measured as a function of accuracy using neurocognitive domains: Symbol Digit Coding, Divided Attention Test (Dual) Sequence Comparison, Matching to Sample, and Pathfinder (Letter and Combined [Number+Letter]). Data were evaluated by ANCOVA with education as a covariate and alpha=.05.

Results: The intent-to-treat population comprised 15 adults. All subjects were included in the MAS XR and placebo groups. Results for accuracy in order of study drug administration were: MAS XR first=MAS XR for 3 weeks, then placebo for 3 weeks; Placebo first=placebo for 3 weeks, then MAS XR for 3 weeks. 1) Symbol Digit Coding-MAS XR first: MAS XR=1.24, placebo=1.18, Placebo first: placebo=1.39, MAS XR=1.28 (F=5.807; p=.035); 2) Divided Attention Test-MAS XR first: MAS XR=92.77, placebo=95.70, Placebo first: placebo=94.30, MAS XR=96.16 (F=4.442; p=.059); 3) Matching to Sample-MAS XR first: MAS XR=95.16, placebo=94.32, Placebo first: placebo=92.64, MAS XR=97.16 (F=6.490; p=.027); 4) Pathfinder Letter-MAS XR first: MAS XR=99.33, placebo=99.50, Placebo first: placebo=99.31, MAS XR=99.93 (F=8.161; p=.016) and 5) Pathfinder Combined-MAS XR first: MAS XR=98.09, placebo=98.81, Placebo first: placebo=97.32, MAS XR=99.23 (F=6.244; p=.03).

Conclusions: Significant improvements on most attention measures occurred on switch from placebo to MAS XR. A practice effect occurred on most measures: subjects who received MAS XR before placebo improved accuracy despite no longer receiving active drug. This suggests an advantage for young adults with ADHD if neurocognitive tasks are performed initially while receiving stimulant treatment.

This study was funded by Shire Pharmaceuticals Inc.

References:

1. Stins JF, Tollenaar MS, Slaats-Willemse DI, et al. Sustained attention and executive functioning performance in attention-deficit/hyperactivity disorder. Neuropsychol Dev Cogn C Child Neuropsychol. 2005;11:285-294.

2. Schoechlin C, Engel RR. Neuropsychological performance in adult attention-deficit hyperactivity disorder: meta-analysis of empirical data. Arch Clin Neuropsychol. 2005;20:727-744.

NR680 Wednesday, May 24, 12:00 PM - 2:00 PM

Circadian Rhythm Disturbances in Adolescents With ADHD

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Educational Objectives:

At the conclusion of this presentation the participant should be able to recognize that severe sleep disturbance may be present in adolescent patients with ADHD and understand that sleep disturbance may affect ADHD symptoms.

Summary:

Introduction. ADHD affects 4-7% of the school-age population. Some evidence suggests significant sleep disturbance in these patients.

Objectives. We hypothesize that ADHD patients will show unstable circadian rhythms, phase delays and seasonal variations in sleep quality compared to control.

Methods. Within 4 weeks of each solstice and equinox, six adolescents with KSADS ADHD and 6 controls are admitted for 4 overnight stays in < 30 lux light conditions. Seventeen Blood samples are drawn at ½ hourly (6PM to 2AM, 8AM to 10 AM and hourly (2AM to 8 AM) intervals to determine melatonin levels by RIA. AW-64 Actiwatches measure activity levels. Initially, the KSADS, ADHD RSIV, Pediatric Sleep Questionnaire are collected. Seasonally a Children's Morning-Eveningness Preferences Scale, and ADHD RSIV are collected. On each admission the ADHD RSIV is given. DLMO and DLMOff are determined from melatonin profiles. Actigraphy data are analyzed for sleep onset, time of awakening, number of times of awakening, total sleep time, and sleep efficiency.

Results. Seven subjects and two controls have entered with seasonal data available for 6 subjects. Five of six ADHD had significant delays in DLMO which correlated with delayed sleep onset. Actigraphy data for subjects A1-A3 demonstrate that sleep onset is significantly delayed, total sleep is reduced and sleep efficiency is poor. Melatonin profiles for A1 demonstrate delay in DLMO and DLMOff. A1's melatonin profiles show a high degree of variability in DLMO (range 11 PM to 2:00 AM). A2's and A3's profiles also indicate a phase shift with significant delays in DLMO and DLMOff and unusual variability (10 PM to 12 PM). ADHD symptomatology (averaged across subjects) was improved (ADHD-RS RCI p<.05) at the summer solstice. **Discussion.** These data are evidence for sleep disruption, phase delays, unstable circadian rhythms, and seasonal effects on circadian rhythm stability and symptomatology in ADHD.

References:

1. Van der Heijden KB et al: Idiopathic chronic sleep onset insomnia in attention deficit/hyperactivity disorder: a circadian rhythm disturbance. Chronobiology Int 2005; 22:559-570.

2. Rybak YE, MacKenzie BE, Levitan RD: Light therapy in adult attention deficit disorder. Chronobiology Int. 2004; 21:802-803.

NR681 Wednesday, May 24, 12:00 PM - 2:00 PM

Efficacy and Safety of Pregabalin for the Treatment of GAD in Elderly Patients

Arifulla Khan, M.D. *Northwest Clinical Research Center, 1900 - 116th Ave NE, Bellevue, WA*, Gail M. Farfel, Ph.D., Jerri D. Brock, M.S., Richard J. Kavoussi, M.D.

Educational Objectives:

This presentation will improve participants' understanding of the anxiolytic efficacy and safety of pregabalin in elderly patients with GAD.

Summary:

Objective: To evaluate the safety and efficacy of pregabalin in relieving the symptoms of GAD in patients ≥65 years of age. **Methods:** Multicenter, randomized, flexible-dose, placebo-controlled, double-blind, parallel-group trial of pregabalin in the treatment of GAD. Patients underwent an 8-week double-blind, flexible-dose (between 150 and 600 mg/d) treatment phase, including a 1-week titration period (50 mg/d to 150 mg/d). The primary efficacy assessment was change from baseline (LOCF) in HAM-A total score. **Results:** Mean age at GAD onset was 56 years; 77% of patients were women; mean age at enrollment was 72 years; mean duration of GAD was 17 years. Mean change from baseline in HAM-A total score was -12.84 (n=177) for the pregabalin group and -10.7 (n=96) for the placebo group (*P*=.0437). The most common adverse events (AEs) among pregabalin-treated patients were dizziness (20.3%), somnolence (13.0%), headache (10.2%), and nausea (9.0%). Most AEs were mild-to-moderate and self-limiting. Discontinuation rates due to AEs were 10.7% and 9.4% in the pregabalin and placebo groups, respectively. **Conclusions:** Pregabalin was effective in reducing the symptoms of GAD in patients aged 65 years and older and was safe and well tolerated in this population.

References:

1. Pohl RB, Feltner DE, Fieve RR, Pande AC. Efficacy of pregabalin in the treatment of generalized anxiety disorder: double-blind, placebo-controlled comparison of BID versus TID dosing. J Clin Psychopharmacol. 2005;25:151-158.
2. Rickels K, Pollack MH, Feltner DE, et al. Pregabalin for treatment of generalized anxiety disorder: a 4-week, multicenter, double-blind, placebo-controlled trial of pregabalin and alprazolam. Arch Gen Psychiatry. 2005;62:1022-1030.

NR682 Wednesday, May 24, 12:00 PM - 2:00 PM

The Development of Korean ADHD Scale

Jinsung Kim, M.D. *Yeunam University Hospital, Daemyung Dong Namgu, Daegu, 705-717, Republic of Korea*, Changjin Song, M.D., Wanseok Seo, M.D., Bonhoon Koo, M.D., Daiseg Bai, Ph.D., Junyeob Lee, M.D., Hyelin Lee, M.D.

Educational Objectives:

To developing of Korean attention deficit hyperactivity disorder scale

Summary:

Purpose of this study is to develop more reliable ADHD behavioral scales in Korea based on Diagnostic and Statistical Manual of Mental Disorder, 4th edition (DSM-IV) criteria. ADHD group (N= 826) and normal group (N=120) were evaluated by four kinds of ADHD scales (Attention Deficit Disorders Evaluation Scale - Home version [ADDES-HV], ADDH Comprehensive Teacher Rating Scale [ACTeRS], Children Attention Profile [CAP], Swanson, Nolan, and Pelham Checklist[SNAP]) and investigated several statistic analysis such as item correlation analysis, factor analysis, multilinear regression analysis, discriminant analysis and measure the reliability, validity. As a result, the 39 items were extracted, and 5 factors were revealed. The factors were restlessness, hyperactivity, difficulty of sustaining attention, impulsivity, difficulty to remain on the task Cronbach's alpha of these factors were 0.857, 0.852, 0.915, 0.887, 0.897, respectively. Discriminant ability of these factors for elementary school aged ADHD patients is 99.15%. To conclude, this new developed 39 items of ADHD behavioral checklist will be a useful screening tool for ADHD symptoms in Korea.

References:

1. Brent RC, Jeneva IO, Kathleen MM: Ten-year review of rating scales. V: scales assessing attention-deficit/hyperactivity disorder. J Am Acad Child Adolesc Psychiatry 2003; 42: 1015-1037.
2. Morgan AE, Hynd GW, Riccio CA, Hall J: Validity of ADHD predominately inattentive type and combined types: Relationship to previous DSM diagnoses/subtype differences. J Am Acad Child Adoles Psychiatry 1996; 35: 325-333.

NR683 Wednesday, May 24, 12:00 PM - 2:00 PM

Aripiprazole Augmentation for Treatment Refractory GAD

Gustavo Kinrys, M.D. *Cambridge Health Alliance - Harvard Medical School, Psychiatry, 1493 Cambridge Street, Cambridge, MA, 02139*, Fernanda Nery, B.A., Eliza Coleman, B.A., Roberto B. Sassi, M.D., Robert T. Dunn, M.D., Lisa Wygant

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize and understand the potential clinical use of aripiprazole as an augmentation strategy in the treatment of GAD.

Summary:

Objectives: GAD is a common distressing and disabling condition affecting 5% of the population. Although a number of therapeutic agents have demonstrated efficacy in the treatment of GAD, many patients (40-65%) remain symptomatic after initial intervention and only a minority experience remission. Aripiprazole is an atypical antipsychotic agent with partial dopaminergic and 5HT 1(A) receptor agonist activity. We assessed the use of aripiprazole as an adjunctive treatment of anxiety among patients with GAD.

Method: 12 patients (mean +/- SD age = 48.9 +/- 10.5 years, 66.7% female) with GAD diagnosed by use of the Structured Clinical Interview for DSM-IV-Axis I Disorders, who had failed to experience a clinical response following an adequate trial of an anxiolytic, were treated with open-label adjunctive aripiprazole for 8 weeks. The main outcome measures were the Hamilton Anxiety Scale (HAM-A), the Clinical Global Impression of Severity (CGI-S), and the Clinical Global Impression of Improvement (CGI-I).

Results: 9/12 (75.0%) patients completed the trial. Using a completer analysis, 8/9 (88.8%) patients were classified as responders. An intent-to-treat (ITT) analysis resulted in 9 responders (75.0%). The overall proportion of remitters (HAM-A ≤ 7) was 7/9 (77.7%) using a completer analysis and 7/12 (58.3%) using the ITT analysis. Common adverse events included sedation, tiredness, agitation, and nervousness.

Conclusions: Results from this pilot and open label study suggest that aripiprazole may effectively augment response to anxiolytic medications in patients with treatment refractory GAD. Further investigation is warranted to confirm these preliminary findings.

References:

1. Jordan S, Koprivica V, Chen R, Tottori K, Kikuchi T, Altar CA.The antipsychotic aripiprazole is a potent, partial agonist at the human 5-HT1A receptor. Eur J Pharmacol. 2002 Apr 26;441(3):137-40.
2. Worthington JJ 3rd, Kinrys G, Wygant LE, Pollack MH. Aripiprazole as an augmentor of selective serotonin reuptake inhibitors in depression and anxiety disorder patients. Int Clin Psychopharmacol. 2005 Jan;20(1):9-11.

NR684 Wednesday, May 24, 12:00 PM - 2:00 PM

Physical Activity in Anorexia Nervosa: Psychological, Behavioral and Biological Correlates

Diane A. Klein, M.D. *Columbia University, Psychiatry, 1051 Riverside Drive, Unit 98, New York, NY, 10032*, Janet Schebendach, M.S., Laurel Mayer, M.D., B. Timothy Walsh, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to appreciate the importance of locomotor activity in anorexia nervosa. The participant should also be able to identify at least two features (behavioral, psychological, and/or biological) associated with elevated levels of physical activity in this disorder.

Summary:

Excessive physical activity is a problematic behavior in many patients with Anorexia Nervosa (AN) that may contribute to pathogenesis of the disorder and is associated with worsened outcome. Much remains unknown about excessive physical activity in AN and about the psychological and biological processes that drive it. The current study was undertaken to determine the psychological and behavioral correlates of locomotor activity among inpatients with AN. We were also interested in determining the relationship between locomotor activity and the stress hormone cortisol. Subjects were 30 women with AN receiving treatment on the GCRU at NYSPI. During the first week of hospitalization and before formal weight gain, locomotor activity was monitored using an accelerometer. Activity measures were compared with psychological ratings, self-reported exercise before hospitalization, and (for 15 patients) 24-hour urinary cortisol collected contemporaneously. Subjects demonstrated individual differences in locomotor activity as assessed by the accelerometer. Twenty-four-hour activity counts were highly correlated with attitude towards exercise as measured by the Commitment to Exercise Scale (Davis, 1994). Forty-four percent of women reported recent "excessive" exercise; activity counts during hospitalization were significantly greater in this group as compared with low-exercisers. There was a significant positive association between activity counts and urinary cortisol levels. These findings lend convergent validity to the presence of a subgroup of women with AN with a higher "drive" for physical activity, both before and during inpatient hospitalization. Abnormalities in HPA axis activity may be related to this process. Further investigation is required to confirm these results.

References:

1. Journal Article - Licinio J, Wong ML, Gold PW. The hypothalamic-pituitary-adrenal axis in anorexia nervosa. Psychiatry Research, 1996 Apr 16;62(1):75-83.
2. Journal Article - Davis C, Kennedy SH, Ravelski E, Dionne M. The role of physical activity in the development and maintenance of eating disorders. Psychological Medicine, 1994 Nov;24(4):957-67.

NR685 Wednesday, May 24, 12:00 PM - 2:00 PM

Annual Payment Comparisons Among Frequently Prescribed ADHD Pharmacotherapies

Maureen Lage, Ph.D. *HealthMetrics Outcomes Reseearch, 120 Anchorage Circle, Groton, CT*, Huabin F. Zhang, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize differences in total direct medical payments associated with alternative ADHD medications and to recognize the factors that help to predict total direct medical payments.

Summary:

Objective: This study examines differences in total direct medical payments (payments) associated with three commonly prescribed pharmacotherapies - extended release methylphenidate (OROS® MPH, CONCERTA®), mixed amphetamine salts extended release (MAS XR, Adderall XR®), and atomoxetine (Strattera®).

Methods: From a large claims database we identified individuals aged 6-17 who were diagnosed with ADHD, initiated therapy with the 1 of the 3 pharmacotherapies (first use identified as 'index date') and were continuously insured from 6 month pre to 12 month post index date. In addition, individuals could not have received any other ADHD medication in the one year post-index date and must have received at least 1 prescription of the intent-to-treat medication during the last 30 days of the 1 year follow-up period. Pair-wise comparisons were restricted for the time period when both drugs were on market: between 10/29/2001 and 4/30/2005 when comparing OROS MPH (N=4,491) to MAS XR (N=5,325); and between 1/4/2003 and 4/30/2005 when comparing OROS MPH (N=1,651) to atomoxetine (N=2,131). Multivariate stepwise regressions were utilized with the log of payments in the 1 year post index date as the dependent variable. The regressions controlled a wide range of factors that may potentially impact payments.

Results: Results reveal that demographic characteristics, general health status, comorbitidities, and timing of medication initiation all impacted payments for individuals diagnosed with ADHD. Controlling for these factors, initiation of OROS MPH was associated with a 22.57% reduction in payments compared to initiation on atomoxetine (from $3141.42 to $2,432.40; $p<0.0001$) and a 4.14% reduction in payments compared to initiation on MAS XR (from $2,729.82 to $2,616.53; $p=0.0052$).

Conclusions: Results demonstrate that among children diagnosed with ADHD the use of OROS MPH is associated with significantly lower payments compared to the use of atomxetine or MAS XR.

References:

1. Leibson CL, Long KH. Economic implications of attention-deficit hyperactivity disorder for healthcare systems. Pharmacoeconomics 2003; 21(17): 1239-62.
2. Marchetta A, Magat R, Lau H, Murphy EL, Jensen PS, Conners CK, Findling R, Wineburg E, Corotenuto I, Einarson TR, Iskedjian M. Pharmacotherapies for attention-deficit/hyperactivity disorder: Expected cost analysis. Clin Ther 2001; 23(11): 1904-21.

NR686 Wednesday, May 24, 12:00 PM - 2:00 PM

ADHD-Specific Quality of Life With Mixed Amphetamine Salts Extended Release in Adults With ADHD

Jeanne Landgraf *Healthact, Inc, 205 Newbury Street, 4th Floor, Boston, MA, 02116*

Educational Objectives:

At the conclusion of this session, participants should be able to discuss changes in ADHD-specific quality of life, as assessed using the AIM-A, among adults with ADHD given up to 10 weeks of psychostimulant therapy with mixed amphetamine salts extended release.

Summary:

Introduction: ADHD in adults negatively impacts multiple life domains. To assess disease-specific quality of life, an adult version of the ADHD Impact Module (AIM-A) has been developed.

Methods: This 10-week interim analysis examined AIM-A findings from the 30-week, ongoing, open-label Quality of Life, Effec-

tiveness, Safety, and Tolerability (QU.E.S.T.) trial of once-daily mixed amphetamine salts extended release (MAS XR) 10-60 mg/d. The trial enrolled adults (aged ≥18 years) with a diagnosis of ADHD in community practice settings who were categorized according to previous treatment status (no previous treatment, NaUïve; previous stimulant treatment, Prev Stim; previous non-stimulant treatment, Prev Nonstim). ADHD-specific quality-of-life findings described here are derived from the AIM-A, which includes scores from 6 domains (Living with ADHD, General Well-being, Performance and Functioning, Relationships and Communications, Bothersomeness and Concern, and Daily Interference).

Results: Intent-to-treat subjects in the NaUïve (n=378), Prev Stim (n=272), and Prev Nonstim (n=52) categories exhibited similar, statistically significant (p<.0001) improvements on all 6 AIM-A quality-of-life domains. Improvements emerged within 2 weeks following initiation of MAS XR treatment and were maintained or gradually increased up to study week 10. For all previous treatment groups, the most robust improvements based on change from baseline to endpoint scores were seen within the Performance and Functioning (35.7), Bothersomeness and Concern (26.0), and the Daily Interference (28.4) domains (all p<.0001). Changes from baseline to endpoint in the other AIM-A domains, including Living with ADHD (12.8), General Well-being (18.0), and Relationships and Communication (18.7), were also statistically significant for each previous treatment group (all p<.0001).

Conclusions: In adults with ADHD, up to 10 weeks of therapy with MAS XR 10-60 mg/d is associated with significant improvements in ADHD-specific quality of life as measured by the AIM-A.

This study was funded by Shire Pharmaceuticals Inc.

References:

1. Murphy K, Barkley RA. Attention deficit hyperactivity disorder in adults: comorbidities and adaptive impairments. Compr Psychiatry. 1996;37:393-401.
2. Landgraf JM. Measuring quality of life in adults with ADHD: preliminary findings with the adult Attention deficit hyperactivity disorder Impact Module (AIM-A). Presented at: American Psychological Association Annual Convention; August 19, 2005; Wa.

NR687 Wednesday, May 24, 12:00 PM - 2:00 PM

The Serotonin Transporter Gene and Anxiety Level in Social Phobia Patients

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that the serotonin transporter gene promotor region polymorphism(5-HTTLPR) may not be associated with the degree of anxiety in social phobia patients.

Summary:

Introduction:

This study investigated the association of the polymorphism of the 5HT transporter gene(SLC6A4, a 44 base pair insertion/deletion in the promoter region, 5-HTTLPR) with the degree of anxiety, in patients with social phobia.

Method:

58 Korean social phobia(SP) patients were recruited. DNA analysis with polymerase chain reaction was used for the genotyping. To evaluates the degree of anxiety, we employed the Korean version of State-Trait Anxiety Inventory Form-Trait(STAI-T) and the Korean version of Beck Anxiety Inventory(BAI). We used analysis of variance(ANOVA) with P-value less than 0.05 being statistically significant.

Results:

Among 58 patients, 6(10.3%) patients showed l/l type, 8(13.8%) patients showed l/s type, and 44(75.9%) patients showed s/s type.

The mean STAI-T scores of l/l, l/s, and s/s type were 59.0±10.5, 57.1±13.1, and 56.3±8.7, respectively. There were no significant differences in the STAI-T scores among genotypes. And the mean BAI scores of l/l, l/s, and s/s type were 25.5±14.6, 26.9±13.9, and 21.6±8.8. Also, there were no significant differences in the BAI scores.

Conclusions:

This study suggests that the 5-HTTLPR polymorphism dose not significantly associate with the degree of anxiety in SP patients. But, we should consider different ethnic backgrounds and small sample size.

Remark : This study is not supported by any commercial funding.

References:

1. K. Peter Lesch, Jens Benninghoff, and Angelika Schmitt: The psychopharmacogenetic-neurodevelopmental interface in serotonergic gene pathways. Pharmacogenetics of Pyschotropic Drugs, edited by Bernard Lerer, Cambridge, Cambridge University Press, 2002.
2. Lesch KP, Bengel D, Heils A, Sabol SZ, Greenberg BD, Petri S, Benjamin J, Muller CR, Hamer DH, Murphy DL: Association of anxiety-related traits with a polymorphism in the serotonin transporter gene regulatory region. Science 1996; 274:1527-1531.

NR688 Wednesday, May 24, 12:00 PM - 2:00 PM

The Impact of Unrecognized Anxiety on Health-Related Quality of Life in Patients With Functional Dyspepsia

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Educational Objectives:

At the conlusion of this session, the participant should understand the relationship between anxiety and functional dyspepsia.

Summary:

Objective: Gastroenterologists have been criticized for under-recognizing and undertreating mental health disorders. This criticism assumes patients with recognized disorders and those with unrecognized disorders suffer the same burden of illness. The current investigation examined the impact of unrecognized anxiety disorders on health-related quality of life(HRQOL) in patients with functional dyspepsia

Methods : 347 functional dyspepsia subjects were recruited from Wonkwang and Catholic university's gastroenterologic clinic. The patient were selected from a population of outpatients who were diagnosed with functional dyspepsia by gastroenteroglogists. The patient completed Spielberger state-trait anxiety inventory(STAI), Nepean dyspepsia index scale-Korean version(NDI-K) and SF-36-Korean version(SF-36-K).

Results : The patient with state anxiety showed significantly lower score in interference, knowledge and sleep disturbance dimensions of NDI-K than the patient without state anxiety as well as showed significantly lower score in each dimension of SF-36-K. There was no significant difference between the patient with trait anxiety and the patient without trait anxiety in NDI-K. In addition, higher state anxiety and/or trait anxiety on the STAI were associated with poorer disease specific HRQOL and general HRQOL.

Conclusion : Patients with functional dyspepsia that have been had unrecognized anxiety appear to suffer from poorer HRQOL than patients without anxiety. This study suggest that we must realize that anxiety likely to be prevalent sources of excess poor general health among patients with functional dyspepsia and that when anxiety strike the patient with functional dyspepsia, these often go unrecognized and untreated.

References:

1. Chenng C, Hui WM, Lam SK. Psychosocial factors and perceived severity of funtional dyspeptic symptoms: A psychosocial interactioninst model. Psychosom Med 2004;66:85-91.
2. Drossman DA, Creed FH, Olden KW, et al. Psychosocial aspects of functional gastrointestinal disorder. Gut 1999;45(suppl II):II25-II30.

NR689 Wednesday, May 24, 12:00 PM - 2:00 PM

Venlafaxine XR in Social Anxiety Disorder: A Pooled Analysis of Response and Remission Rates

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Educational Objectives:

1. Compare the efficacy of venlafaxine XR compared with placebo in the treatment of SAD
2. Evaluate the effects of gender on response to treatment of SAD with venlafaxine XR or placebo
3. Assess the effects of physical symptoms on response to treatment of SAD with venlafaxine XR or placebo

Summary:

Objective: Compare the efficacy of venlafaxine extended release (XR) versus placebo for treatment of social anxiety disorder (SAD).

Methods: Data were pooled from 5 randomized studies of patients with DSM-IV SAD (ITT n=1459) treated with venlafaxine XR (75-225 mg/d) or placebo for 12 weeks; 1 study lasted 28 weeks. Response (Clinical Global Impressions-Improvement score ≤2) and remission (Liebowitz Social Anxiety Scale score ≤30) rates were calculated for the overall population, and stratified by gender and physical symptom severity (based on Social Phobia Inventory sweating, blushing, palpitations, and tremor items), and compared between groups using the Fisher exact test (last observation carried forward). The number needed to treat (NNT) was calculated using week 12 remission rates.

Results: Overall week 12 response rates were 55% for venlafaxine XR and 33% for placebo ($P<0.0001$); remission rates were 25% and 12%, respectively ($P<0.0001$). Findings for men, women, and patients with varying physical symptom severity were consistent with those in the overall population. Week 28 response rates for venlafaxine XR and placebo were 58% and 33%, respectively ($P<0.0001$); remission rates were 31% and 16%, respectively ($P=0.0023$). The NNT was 8 (95% CI: 6.5, 8.9).

Conclusion: Venlafaxine XR effectively treats SAD, regardless of gender or severity of physical symptoms.

References:

1. Liebowitz MR, Gelenberg AJ, Munjack D: Venlafaxine vs paroxetine in social anxiety disorder. Arch Gen Psychiatry 2005; 62:190-198.
2. Liebowitz MR, Mangano RM, Bradwejn J, Asnis G: A randomized controlled trial of venlafaxine extended release in generalized social anxiety disorder. J Clin Psychiatry 2005; 66:238-247.

NR690 Wednesday, May 24, 12:00 PM - 2:00 PM

Dermal Response to Methylphenidate Transdermal System in Pediatric Subjects

Frank A. Lopez, M.D. *Childrens Development Center, 600 South Orlando Avenue, Suite 102, Maitland, FL, 32751*, Robert L. Findling, M.D., Maryann Livolsi, R.N.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to:

Describe the clinical use of the methylphenidate transdermal system (MTS) in pediatric subjects.

Discuss the clinician-based assessments of dermal response, discomfort and adherence of MTS in a naturalistic study.

Summary:

Objective: To assess the dermal response of methylphenidate transdermal system (MTS) compared with placebo transdermal system (PTS).

Method: This was a randomized, double-blind, double-dummy, parallel-group, placebo-controlled, naturalistic study. Two hundred seventy-four (274) children aged 6-12 years diagnosed with ADHD using DSM-IV-TR criteria were enrolled and received study medication. Transdermal patches were applied each morning and worn for 9 hours each day over 7 weeks. Dermal effects were measured using three scales. Skin responses were scored from 0 to 7, in which 0 represented no irritation and 7 represented a strong reaction beyond the test site. Scores between these endpoints included gradations of Extended Release ythema, edema and papules. Skin discomfort was scored from 0 to 3, in which 0 represented no discomfort and 3 represented severe intolerable discomfort. Patch adherence was scored from 0 to 4, in which 0 meant that greater than 90% of the patch remained adhered to the skin and 4 represented complete detachment of the patch.

Results: At the final study site visit, 74.4% of subjects receiving MTS treatment reported either no irritation or mild Extended Release ythema. Mild Extended Release ythema was an expected outcome of patch application and generally dissipated within 24 hours. Either no discomfort or mild skin discomfort resulting from patch wear was reported in 94.5% of subjects. After an approximately 9-hour wear time, 77.6% of subjects reported that patches were still well adhered to the skin (ie, greater than 75% of the patch remained completely adhered to the skin). In 17.7% of subjects, patch adherence could not be assessed, due to patch removal that occurred prior to the study site visit per protocol.

Conclusion: Application of MTS resulted in no or mild skin irritation or discomfort, and patches adhered well to the skin for the majority of the subjects.

Supported by funding from Shire US Inc.

References:

1. Findling RL, Lopez FA. The effects of transdermal methylphenidate with reference to OROS methylphenidate in ADHD. Poster presented at the joint meeting of AACAP and CACAP. Toronto, Ontario. October 20, 2005.
2. Wigal S, McGough JJ, Abikoff H, Turnbow JM, Posner K, Moon E. Behavioral effects of methylphenidate transdermal system in children with ADHD. Poster presented at the joint meeting of AACAP and CACAP. Toronto, Ontario. October 21, 2005.

NR691 Wednesday, May 24, 12:00 PM - 2:00 PM

Improvement in Anxiety Symptoms in Bipolar Depression With Quetiapine Monotherapy: Results From Two Placebo-Controlled Studies

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Educational Objectives:

At the conclusion of this session, the participant should be able to understand the role of quetiapine monotherapy in the treatment of anxiety symptoms in bipolar depression.

Summary:

Objective: To evaluate the efficacy and tolerability of quetiapine monotherapy for anxiety symptoms in patients with bipolar I or II depression.[1,2]

Methods: A post-hoc analysis of anxiety symptoms in 1045 patients with bipolar I or II depression (DSM-IV) from two double-blind, randomized, placebo-controlled 8-week studies of quetiapine (300 or 600 mg/d; once-daily, evening dosing) was conducted. Anxiety symptoms were assessed weekly using HAM-A total scores, and HAM-A psychic (items 1-6, 14) and somatic anxiety (items 7-13) factor scores. Change from baseline in these scores at each assessment were evaluated using mixed-effect model, repeated-measures analysis.

Results: Mean baseline HAM-A total scores were similar across the treatment groups (18.6-18.9). There was a significantly greater improvement from baseline in mean HAM-A total scores at the first evaluation (Week 1) in both quetiapine groups compared to placebo (change from baseline 300 mg/d: -4.59, $P<0.001$; 600 mg/d: -4.10, $P=0.003$ versus placebo: -2.77). These improvements were sustained through to Week 8 with both quetiapine doses (300 mg/d: -10.12 and 600 mg/d: -10.48; both $P<0.001$ versus placebo: -6.88). The effect sizes for quetiapine 300 and 600 mg/d were 0.56 and 0.62, respectively. At Week 8, there were also significant improvements from baseline in HAM-A psychic and somatic anxiety factor scores with quetiapine 300 (both $P<0.01$) and 600 mg/d (both $P<0.001$) compared to placebo. Common adverse events included dry mouth (300 mg/d: 43.4%; 600 mg/d: 43.7%; placebo: 12.7%), sedation (30.9%, 29.9%, 8.1%), and somnolence (28.6%, 27.0%, 6.6%).

Conclusions: Quetiapine monotherapy is significantly more effective than placebo and generally well-tolerated for the treatment of anxiety symptoms associated with bipolar depression.

Supported by funding from AstraZeneca Pharmaceuticals LP.

References:

1. Post RM, Leverich GS, Altshuler LL, Frye MA, Suppes TM, Keck PE, et al. An overview of recent findings of the Stanley Foundation Bipolar Network (Part I). Bipolar Disord 2003;5(5):310-19.

2. American Psychiatric Association. Practice guideline for the treatment of patients with bipolar disorder (revision). Am J Psychiatry 2002;159(4 Suppl):1-50.

NR692 Wednesday, May 24, 12:00 PM - 2:00 PM

Family-Based Association Between TPH2, ADHD and Performance on a Continuous Performance Test (TOVA)

Iris Manor *Geha Mental Health Center, Geha Mental Health Center, Petach Tiqva, 49100, Israel*, Richard P. Ebstein, Sheera Meidad, Jacque Eizenberg, Zvi Zemishlany, Sam Tyano

Educational Objectives:

Whereas most studies have stressed the importance of dopamine due to the efficacy of methylphenidate in treatment of this disorder, the current report focuses attention on a particular serotonergic gene. So far three reports now provide evidence that TPH2 coding for a key enzyme in the serotonin pathway confers risk for ADHD, suggesting the possibility that the serotonergic pathway might be a potential drug target in this disorder.

Summary:

Background: Tryptophan hydroxylase (TPH) catalyzes the rate limiting step in 5-HT synthesis. Recently, a second TPH gene was identified in the genome of humans, mice, and rats, called TPH2. This gene is predominantly expressed in the brain stem, while the classical TPH gene, now called TPH1, is expressed in the gut, pineal gland, spleen, and thymus. Several reports have found association between SNPs in the TPH2 genomic region and affective disorders (major depression & suicide). Additionally, two reports recently observed association between this gene and ADHD.

Methods: We genotyped 8 SNPs (rs1386488, rs2220330, rs1386495, rs1386494, rs6582072, rs1386492, rs4760814 & rs1386497) in the TPH2 region towards verifying the reported association between this gene and ADHD and further examined association with scores on a CPT (TOVA) . Association between single SNPs and haplotypes was tested using FBAT and UNPHASED. 271 probands and their parents (161 families) were genotyped.

Results: Six SNPs showed association with ADHD ($p<0.05$). When all 8 SNPs were included in the haplotype analysis, the most common haplotype (80%) was significantly under transmitted to probands (FBAT: z=-2.012, p= 0.044) whereas the second most common haplotype was preferentially transmitted (FBAT: z=2.087, p= 0.036). Similar results were obtained using UNPHASED (chi-square=4.357; p=0.036; transmitted=39, not-transmitted=21; chi-square=3.29, p=0.069; transmitted=43, not-transmitted=64). Association was also observed between a six locus SNP haplotype and total Extended Release rors of omission (TOVA): z=1.986, p= 0.047.

Conclusions: This report confirms and extends two previous investigations that TPH2 contributes risk to ADHD. Additionally, association was observed between TPH2 and Extended Release rors of omission (TOVA) suggesting that the risk by this gene for ADHD is mediated by neuropsychological mechanisms related to attentional processes

References:

1. Walitza S, Renner TJ, Dempfle A, Konrad K, Wewetzer C, Halbach A,.

2. Sheehan K, Lowe N, Kirley A, Mullins C, Fitzgerald M, Gill M, Hawi.

NR693 Wednesday, May 24, 12:00 PM - 2:00 PM

Tolerability of Mixed Amphetamine Salts Extended Release in Young Girls With ADHD

James J. McGough *UCLA Neuropsychiatry Institute, 300 UCLA Medical Plaza, Los Angeles, CA, 90095*

Educational Objectives:

At the conclusion of this session, participants should be able to...

Identify common adverse events reported in girls aged 6 to 12 years with attention-deficit/hyperactivity disorder given therapy with mixed amphetamine salts extended release (MAS XR) 10-30 mg/d

Recognize that the tolerability of MAS XR in young girls is similar to that of psychostimulant therapy in other patient populations

Summary:

Introduction: Few studies have examined the tolerability of psychostimulant treatment in young girls with ADHD.

Methods: A 3-week randomized, placebo-controlled, double-blind, parallel-group trial was conducted in girls aged 6 to 12 years with ADHD. Subjects were administered placebo (n=57) or mixed amphetamine salts extended release (MAS XR) 10 mg/d (n=28), 20 mg/d (n=26), or 30 mg/d (n=26). Tolerability was assessed

based on frequency and intensity of spontaneously reported adverse events.

Results: A total of 164 adverse events were reported during the study; most (95%) were mild or moderate in intensity and expected based on observations with other psychostimulants. The most commonly reported adverse events with MAS XR or placebo were headache (23.8% and 49.1%, respectively), abdominal pain (20.0% and 22.8%, respectively), insomnia (22.5% and 3.5%, respectively), anorexia (18.8% and 3.5%, respectively), and infection (11.3% and 5.3%, respectively). Frequencies of abdominal pain, anorexia, and weight loss were greater with increasing MAS XR dose. One serious adverse event (constipation) was seen in a subject given MAS XR 30 mg/d, but this was considered unrelated to study medication. Few subjects discontinued because of an adverse event (placebo [n=1], weight gain; MAS XR 10 mg/d [n=1], dizziness; MAS XR 20 mg/d [n=1], unable to swallow pills; MAS XR 30 mg/d [n=1], stomach pain). The adverse events associated with MAS XR were mild or moderate in intensity and resolved during follow-up.

Conclusions: In young girls with ADHD, MAS XR 10-30 mg/d was generally well tolerated. The adverse events associated with MAS XR in this study are consistent with those historically observed with psychostimulant therapy.

This study was funded by Shire Pharmaceuticals Inc.

References:

1. McCracken JT, et al. Analog classroom assessment of a once-daily mixed amphetamine formulation, SLI381 (Adderall XR), in children with ADHD. J Am Acad Child Adolesc Psychiatry. 2003;42:673.
2. West SA, et al. The GRACE Study: an evaluation of girls, Ritalin, and ADHD. Poster presented at: Annual Meeting of the American Academy of Child and Adolescent Psychiatry; October 19-24, 2004; Washington, DC.

NR694 Wednesday, May 24, 12:00 PM - 2:00 PM

Adverse Event Adaptation With Mixed Amphetamine Salts Extended Release in Children

James J. McGough *UCLA Neuropsychiatry Institute, 300 UCLA Medical Plaza, Los Angeles, CA, 90095*

Educational Objectives:

At the conclusion of this session, participants should be able to:

- Describe how the frequency of certain reported adverse events decreases over time in children 6 to 12 years old with attention-deficit/hyperactivity disorder receiving mixed amphetamine salts extended release (MAS XR) 10-30 mg/day
- Recognize the possible adaptation effect of adverse events in children receiving MAS XR

Summary:

Introduction: Objective data supporting improved tolerability over time with psychostimulant treatment in children being treated for ADHD are lacking.

Methods: This was a 3-week, randomized, placebo-controlled, double-blind, parallel-group trial. Children aged 6-12 years with ADHD (predominantly hyperactive-impulsive or combined subtype) were assigned to receive placebo (n=210) or mixed amphetamine salts extended release (MAS XR) 10-30 mg/d (n=374). The weekly frequency of anorexia, abdominal pain, headache, emotional lability, insomnia, and nervousness was determined.

Results: Overall frequency of these 6 adverse events decreased from week 1 (MAS XR, 39.3%; placebo, 19.0%) to week 3 (MAS XR, 11.0%; placebo, 8.0%). Among subjects who prematurely discontinued the study, few withdrew because of an adverse event (MAS XR, 9 of 374[2.4%];placebo, 6 of 210[2.9%]). Anorexia, emotional lability, insomnia, and nervousness were more frequent with MAS XR than with placebo, but decreased from week 1 (13.4%, 6.1%, 9.1%, 2.7%, respectively) to week 3 (2.9%, 1.2%, 3.2%, 1.7%, respectively). During weeks 1 through 3, abdominal pain was reported more frequently in MAS XR subjects (9.9%, 4.4%, 4.3%, respectively) than in placebo subjects (4.8%, 3.1%, 1.1%), but decreased over time for both groups. Throughout the study, headache was comparable between the groups and showed similar decreases with MAS XR (weeks 1, 2, and 3: 11.5%, 7.5%, 3.5%, respectively) or placebo (weeks 1, 2, and 3: 12.9%, 9.9%, 5.7%, respectively).

Conclusions: Adverse event frequency decreased over a 3-week treatment period in children with ADHD who were administered MAS XR 10-30 mg/d, and only 2.4% of subjects withdrew because of an adverse event. The possible adaptation to adverse events suggests physician communication and patient support during initial MAS XR therapy can facilitate medication adherence.

This study was funded by Shire Pharmaceuticals Inc.

References:

1. McGough JJ, et al. Long-term tolerability and effectiveness of once-daily mixed amphetamine salts (Adderall XR) in children with ADHD. J Am Acad Child Adolesc Psychiatry. 2005;44:530.
2. Greenhill LL, et al. Impairment and deportment responses to different methylphenidate doses in children with ADHD: the MTA titration trial. J Am Acad Child Adolesc Psychiatry. 2001;40:180.

NR695 Wednesday, May 24, 12:00 PM - 2:00 PM

Clinician Rated Effects of MTS and OROS Methylphenidate in Pediatric ADHD

Raun Melmed, M.D. *The Melmed Center, 5020 E Shea Blvd Suite 100, Scottsdale, AZ, 85254*, L Eugene Arnold, M.D., John Burnside, M.D., Robert L. Findling, M.D., Maryann Livolsi, R.N.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to:

Describe the clinical use of the methylphenidate transdermal system (MTS) in pediatric subjects.

Discuss the clinician-based ratings of efficacy of MTS as compared with placebo in a naturalistic setting study.

Summary:

Objective: Evaluate the efficacy of the methylphenidate transdermal system (MTS), compared with placebo, using OROS methylphenidate as a reference therapy, in a naturalistic community setting using clinician-based assessments.

Method: This was a randomized, double-blind, placebo-controlled, parallel-group study with a 5-week dose optimization phase and 2-week maintenance phase. Children aged 6-12 years diagnosed with ADHD by DSM-IV-TR criteria were enrolled. The primary efficacy outcome measure was the ADHD-Rating Scale-IV (ADHD-RS-IV), administered at each study visit beginning with the baseline visit. Subscales for inattentiveness and hyperactivity/impulsivity were used to assess behavior.

Results: The change from baseline to study endpoint in mean ADHD-RS-IV inattentiveness subscale score was -12.4 (±0.78), -11.0 (±0.81), and -5.2 (±0.83), for MTS, OROS methylphenidate, and placebo, respectively. The change from baseline to study endpoint in mean ADHD-RS-IV hyperactivity/impulsivity subscale score was -11.8 (±0.73), -10.6 (±0.76), and -5.2 (±0.78) for MTS, OROS methylphenidate, and placebo, respectively. For both subscales, the change from baseline was statistically significant for MTS and OROS methylphenidate ($p<0.0001$) compared to placebo. At study endpoint, a greater than 30% reduction in ADHD-RS scores was observed in 77.6%, 66.3%, and 28.7% of subjects

treated with MTS, OROS methylphenidate, and placebo, respectively.

Conclusion: Treatment with MTS resulted in statistically and clinically significant improvements in clinician-rated behavior and attention compared with placebo. The efficacy and adverse events profile of MTS was similar to that observed for OROS methylphenidate. MTS may be an effective alternative to oral medications for the treatment of ADHD in children.

Supported by funding from Shire US Inc.

References:

1. DuPaul GJ, Powers TJ, Anastopolous, Reid R. ADHD Rating Scale-IV: Checklists, Norms, and Clinical Interpretation. New York, Guilford Press, 1998.
2. Findling RL, Lopez FA. The effects of transdermal methylphenidate with reference to OROS methylphenidate in ADHD. Poster presented at the joint meeting of the AACAP and CACAP. Toronto, Ontario. October 20, 2005.

NR696 Wednesday, May 24, 12:00 PM - 2:00 PM

Open Label Trial of Aripiprazole in Patients With Treatment Resistant GAD

Matthew A. Menza, M.D. *Robert Wood Johnson Medical School, D207A, 671 Hoes Lane, Piscataway, NJ, 08854*, Roseanne DeFronzo Dobkin, Ph.D., Humberto Marin, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to discuss the use of aripiprazole in patients with treatment resistant GAD.

Summary:

GAD (GAD), with a lifetime prevalence rate of 4 to 6%, tends to be chronic and is frequently sub-optimally responsive to standard pharmacotherapy. The neural circuitry mediating anxiety involves systems utilizing a variety of neurotransmitters, including dopamine. Because of the putative involvement of dopamine in anxiety, the atypical antipsychotics are being investigated in anxiety disorders and have shown some efficacy in PTSD, OCD and GAD. The atypical antipsychotic aripiprazole, a partial agonist of D2 and 5-HT 1A receptors and an antagonist at 5-HT 2A receptors, has not yet been evaluated in patients with GAD.

To examine the efficacy and tolerability of aripiprazole as an adjunctive treatment for patients with GAD, we completed a six-week, open-label, pilot study. After signing informed consent, patients meeting entry criteria - GAD sub-optimally responsive (HAM-A >14) to a full trial of an antidepressant - were treated with flexible dose aripiprazole, beginning at 10 mg/day. The primary outcomes were measures of anxiety symptoms (HAM-A) and overall improvement (CGI). The secondary outcomes were depression (HDRS) and quality of life (Rand SF-36).

Of the 9 (3M, 6F) patients who were enrolled, 8 completed the study; one terminated early due to akathisia.. The mean age was 35 years. Both primary outcomes were significantly improved from baseline to endpoint: 1. anxiety [$F(1,8)=47.13$, $p<.001$], using a repeated measures ANOVA (LOCF), 2. 89% of patients were rated as much improved (CGI=2) or very much improved (CGI= 1) at the end of the study. Secondary outcomes of depression and SF-36 were also significantly improved.

This suggests that aripiprazole may be a useful adjunctive treatment for patients with GAD who are sub-optimally responsive to antidepressants. This approach is consistent with a growing body of work suggesting that a symptom-based treatment (versus category-based) approach to partial response is useful.

References:

1. Adson DE, Kushner MG, Fahnhorst TA. Treatment of residual anxiety symptoms with adjunctive aripiprazole in depressed patients taking selective serotonin reuptake inhibitors. J Affect Disord. 2005 May;86(1):99-104.
2. Pezze MA, Feldon J. Mesolimbic dopaminergic pathways in fear conditioning. Prog Neurobiol. 2004 Dec;74(5):301-20.

NR697 Wednesday, May 24, 12:00 PM - 2:00 PM

Dopamine Transporter (DAT1) Genotype and Response to Methylphenidate in Adults With ADHD

Eric Mick, Sc.D. *Massachusetts General Hospital, 55 Fruit Street, Warrent 705, Boston, MA, 02114*, Joseph Biederman, M.D., Thomas Spencer, M.D., Stephen V. Faraone, Ph.D., Pamela Sklar, M.D.

Educational Objectives:

At the end of the presentation, participants will have an understanding of the relationship between the dopamine transporter gene and response to methylphenidate in adults with ADHD

Summary:

Objective. A polymorphism in the dopamine transporter gene (DAT1) has been previously associated with ADHD and methylphenidate has been hypothesized to block the DAT. The goal of this study was to examine whether DAT1 genotype moderates response and adverse effects associated with treatment with methylphenidate in adults with ADHD.

Methods. Subjects were adults with ADHD (N=xx) enrolled in two identical six-week randomized placebo-controlled parallel design trials of OROS-methylphenidate and immediate release methylphenidate. Subjects were stratified by DAT1 genotype and measures of improvement in ADHD symptoms, rate of clinical response and adverse effects were compared at baseline and study endpoint.

Results. Fifty-nine percent (N=39) of subjects had the homozygous 10/10-repeat genotype, 36% (N=24) had the heterozygous 9/10-repeat genotype, and 5% (N=3) had the homozygous 9/9-repeat genotype. The rate of response to methylphenidate was not statistically or clinically significantly different in these groups (77%, 71%, and 67% responded, respectively p=0.8). Likewise there was no difference in any adverse effects based upon the DAT1 genotype.

Conclusions. DAT1 genotype does not seem to exert meaningful effects on response or adverse effects associated with treatment with methylphenidate in adults with ADHD. Because of the relatively modest sample size, more work with larger samples is needed to confirm these results

References:

1. Spencer T, Biederman J, Wilens T, Faraone SV, Doyle RD, Surman C, et al (2005a): A large, double-blind, randomized clinical trial of methylphenidate in the treatment of adults with attention-deficit/hyperactivity disorder. Biol Psychiatry 57:456-63.
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NR698 Wednesday, May 24, 12:00 PM - 2:00 PM

Assessing the Validity of the Quality of Life Enjoyment and Satisfaction Questionnaire in Adults With ADHD

Eric Mick, Sc.D. *Massachusetts General Hospital, 55 Fruit Street, Warren 705, Boston, MA, 02114*, Joseph Biederman, M.D., Stephen V. Faraone, Ph.D., Thomas Spencer, M.D.

Educational Objectives:

At the end of this presentation, participants will have an understanding of the validty and utility of the Q-LES-Q in the assessment of quality of life in adults with ADHD.

Summary:

Objective.

Despite documentation of robust clinical response to pharmacotherapy of ADHD in adults, the impact of treatment on overall quality of life has not been fully addressed. We assessed the psychometric properties of the Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q) in ADHD adults.

Methods.

179 ADHD and 117 non-ADHD adults from a case control study and 112 adults randomized to placebo or methylphenidate were assessed the Q-LES-Q and the Social Adjustment Scale (SAS). Internal consistency of the 16 individual items Q-LES-Q was assessed with Chronbach's alpha statistic and concurrent validity was assessed via correlation with the SAS total T-score. Response to change was estimated by comparing change in Q-LES-Q scores in responders and non-responders in our randomized clinical trial.

Results

There was no difference in ADHD cases and controls in sex (53% and 44% male, p=0.1) but controls were significantly younger than cases (30.1+/-8.8 versus 36.1+/-10.7 years, p<0.001). ADHD clinical trial patients were comparable to ADHD family study cases (52% male and 37.2+/-9.5 years of age). Internal consistency of the Q-LES-Q items was excellent in ADHD cases (alpha=0.90) and ADHD clinical trials patients (alpha=0.91 at endpoint). Correlation between the Q-LES-Q total score and the SAS total T-score were high in ADHD cases (0.71) and ADHD clinical trial patients (0.61). Compared to non-ADHD controls, ADHD cases had statistically significantly poorer scores on the QLES-Q (52.1+/-10.6 versus 61.7+/-6.8, p<0.001). These values were comparable in the non-responders and responders from the controlled trial of methylphenidate (57.4+/-8.3 versus 64.2+/-7.2, p<0.001).

Conclusions

These results support the validity of the Q-LES-Q as a measure of quality of life in samples of adults with ADHD. Thus, the Q-LES-Q is an appropriate tool to measure quality of life in clinical trials of ADHD adults.

References:

1. Endicott, J., J. Nee, et al. (1993). "Quality of life enjoyment and satisfaction questionnaire: A new measure." Psychopharmacology Bulletin 29(2): 321-326.
2. Spencer, T., J. Biederman, et al. (2005). "A large, double-blind, randomized clinical trial of methylphenidate in the treatment of adults with attention-deficit/hyperactivity disorder." Biological Psychiatry 57(5): 456-63.

NR699 Wednesday, May 24, 12:00 PM - 2:00 PM

Comorbidity of Alcohol Dependence and Substance Dependence With ADHD

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to diagnose and treat adult patients with alcohol dependence and multiple substance addiction with comorbidity of Attention-deficit/hyperactivity disorder (ADHD).

Summary:

ADHD (ADHD) is of great clinical importance not only because of its high prevalence but also due to the frequent comorbid illnesses that are connected with this disorder. Several studies were able to demonstrate that ADHD constitutes a significant risk factor for the exacerbation of habit-forming illnesses, i.e. addictions.

We conducted a study with 152 adult patients with alcohol dependence (n=91), respectively, multiple substance addiction (n= 61) to determine whether or not these patients were affected by ADHD. 20,9% (WURS), respectively, 23,1% (DSM-IV criteria) of the alcohol-dependent patients showed evidence of retrospective ADHS affliction in childhood. With the help of CAARS ADHD was proved persistent in 26,3% of the adult patients. In the group of substance-addicted patients 50,8% (WURS), respectively, 54,1% (DSM-IV) presented with diagnostic criteria for ADHS in childhood and 65,5% (CAARS) showed evidence of ADHD persisting in adult age.

These results reveal that habit-forming illnesses can be associated with a high comorbidity with ADHD, expressed in the form of alcohol abuse and also in the consumption of illegal drugs. The results underline the great importance of early and adequate diagnostics and therapy of ADHD for the prevention of habit-forming illnesses.

References:

1. Biederman J, Wilens TE, Mick E, Faraone SV, Spencer T. Does attention-deficit hyperactivity disorder impact the developmental course of drug and alcohol abuse and dependence?. Biol Psychiatry 1998; 44: 269-273.
2. Wilens TE, Biederman J, Alcohol, drugs, and attention-deficit/hyperactivity disorder: a model for the study of addictions in youth. J Psychopharmacol. 2005 Sep 20.

NR700 Wednesday, May 24, 12:00 PM - 2:00 PM

Stimulant Use in Adults With ADHD

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Educational Objectives:

At the conclusion of this session, the participant should be able to describe factors associated with selection of extended-release versus immediate-release stimulants in the community treatment of adults with attention-deficit/hyperactivity disorder (ADHD).

Summary:

Objective: To compare the demographic and clinical characteristics of adult patients with ADHD who initiate extended-release (ER) versus immediate-release (IR) stimulant medications.

Method: Analysis of claims data from commercially-insured (Pharmetrics, 2000-2004) adult patients, ages 18 to 64 years, who initiate stimulants for ADHD. Comparisons are presented of patient demographic and clinical characteristics during the six-month period prior to starting Extended Release (N=3,416) or IR (N=4,835) stimulants.

Results: Approximately 4 in 10 (41.4%) adults with ADHD started Extended Release stimulants. Patients starting Extended Release and IR stimulants did not significantly differ with respect to gender (% Male: Extended Release : 58.6% versus IR: 58.4%, χ^2=0.03, df=1, p=.86) or specialty of the prescribing physician (% Psychiatrist: Extended Release : 30.7% versus IR: 31.5%; χ^2= 3.9, df=2, p=.15). However, as compared with patients who started IR stimulants, those starting Extended Release stimulants were slightly younger [mean=31.1 years (SD=12.2) versus 32.6 years (SD=12.2), t=5.8, df=8,249, p<.0001]. Extended Release patients were also more likely than IR patients to be diagnosed with ADHD with hyperactivity (ER: 44.1% versus IR: 39.5%, χ^2=30.2, df=1,

p<.0001); to use inpatient (ER: 2.7% versus IR: 1.8%; χ^2=6.4, df= 1, p=.01) and emergency department (ER: 3.0% versus IR: 2.2%; χ^2=4.3, df=1, p=.04) mental health services; and to be treated for a substance use disorder (ER: 6.5% versus IR: 5.2%; χ^2=6.8, df=1, p=.009) during the six-months prior to initiating stimulant treatment.

Conclusions: Extended-release stimulants are commonly used in the community treatment of adults with ADHD. Patients initiating extended-release stimulants tend to demonstrate slightly more pronounced ADHD symptoms than those initiating immediate-release stimulants.

References:

1. Faraone SV, Spencer TJ, Montano B Biderman J: Attention-deficit/hyperactivity disorder in adults: a survey of current practice in psychiatry and primary care. Arch Inter Med 2004;164:1221-1226.
2. Spencer T, Biederman J, Wilens T, et al: A large, double-blind, randomized clinical trial of methylphenidate in the treatment of adults with attention-deficit/hyperactivity disorder. Biol Psychiatry 2005; 57:456-463.

NR701 Wednesday, May 24, 12:00 PM - 2:00 PM

Memory and Executive Function in OCD Patients With Checking Versus Washing Symptoms

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand the differences in neuropsychological findings between clinical subtypes of OCD, 'Washers' and 'Checkers'.

Summary:

Objective : Neuropsychological studies of OCD have described memory and attentional deficits, but these reports have largely ignored the possibility that cognitive disturbances will vary across clinical subtypes. The purpose of the present study was to determine whether 'Washers' and 'Checkers' demonstrate differences in their memory and executive functions. *Method* : Fifty-three outpatients with primary DSM-IV diagnosis of OCD with typical washing (n=26) and checking (n=27) rituals participated in the study. Patients were recruited through the OCD clinic of the Nagoya City University Hospital between October 2001 and June 2005. Each group was administered the Wechsler Memory Scale-Revised (WMS-R) and comprehensive neuropsychological battery to assess attention and executive functioning. Various neuropsychological tests examing attention and executive functioning were subjected to factor analysis. Obtained factor scores were compared between 'Washers' and 'Checkers'. Effect of there factor scores on memory by OCD subtypes were examined by analysis of covariance. The protocol had been approved by the ethics committee of Nagoya City University Medical School, and written consent was obtained from all participants. *Results* : No significant difference in terms of demographic and clinical variables, including symptom severity, was found between the two groups. Three factors, inhibitory attention, sustained attention, and divided attention, were obtained. No significant differences were found in memory and these factor scores between the two groups. Only among 'Checkers', a significant interaction was noted between the inhibitory attention factor and the group for the general memory, while no such interaction among 'Washers'. *Conclusions* : Among 'Checkers', inhibitory attention regulates memory. Results of this study indicate that different obsessive compulsive symptom is mediated by relatively distinct components of cognitive function.

References:

1. Muller J, Roberts JE:Memory and attention in Obsessive-Compulsive Disorder: a review. J Anxiety Disord 2005; 19:1-28.
2. Savage CR, Deckersbach T, Wilhelm S, Rauch SL, Baer L, Reid T, Jenike MA:Strategic processing and episodic memory impairment in obsessive compulsive disorder.Neuropsychology 2000; 14:141-51.

NR702 Wednesday, May 24, 12:00 PM - 2:00 PM

A Preliminary Study of Relationships Between the Young Mania Rating Scale and Clinical Global Impressions Scale in Adolescents With Bipolar Disorder

Danielle Patrick *Cincinnati, OH*, Nick C. Patel, Ph.D., Melissa P. DelBello, M.D., Stephen M. Strakowski, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand how the Young Mania Rating Scale corresponds with clinician judgment in adolescents with bipolar disorder and to recognize the importance of using empirically-derived cutoffs to define response in pediatric and adolescent clinical trials.

Summary:

Objective: To evaluate Young Mania Rating Scale (YMRS) scores, and percent change in baseline YMRS scores, in relation with the Clinical Global Impressions Scale for Bipolar Disorder Improvement (CGI-I) scores from treatment trials of adolescent bipolar disorder.

Methods: Data from a randomized, double-blind, placebo-controlled study of quetiapine with divalproex versus divalproex alone (N=30), a randomized, double-blind, parallel-group study of quetiapine versus divalproex (N=50), an open-label study of olanzapine (N=20), and an open-label study of lithium (N=27) were used. Severity of manic symptoms was assessed at baseline and weekly thereafter using the YMRS, and overall level of improvement was assessed beginning on day 7 and weekly thereafter using the CGI-I. Assessments were completed separately without any dependence on ratings from the alternate rating scale or specific order. Analysis of variance was used to compare endpoint YMRS scores based upon stratification of endpoint CGI-I scores. Receiver Operator Characteristic curves were used to evaluate the ability of the YMRS scores to predict the level of global improvement of symptoms as rated by clinicians.

Results: Mean endpoint YMRS scores significantly differed between groups stratified by endpoint CGI-I score (p<0.001). An endpoint YMRS score of 12.5 and a 56% reduction in baseline YMRS scores represent optimal sensitivity and specificity in classifying responders and non-responders.

Conclusion: Our preliminary results demonstrate that YMRS scores correspond with the level of global improvement in adolescents with bipolar disorder. Currently used cutoffs to define response in adolescent bipolar disorder research may be appropriate with regard to sensitivity and specificity. Studies with methods specific to evaluate and compare these rating scales and larger patient samples from multiple sites are needed to confirm these findings.

Acknowledgments: This study was supported by grants from the AstraZeneca Pharmaceuticals (MPD), Eli Lilly and Company (MPD), Klingenstein Third Generation Foundation (MPD), and NIMH (MH63373, MPD).

References:

1. Young RC, Biggs JT, Ziegler VE, Meyers DA: A rating scale for mania: reliability, validity and sensitivity. Br J Psychiatry 1978; 133:429-435.

2. Spearing MK, Post RM, Leverich GS, Brandt D, Nolen W: Modification of the Clinical Global Impressions (CGI) Scale for use in bipolar illness (BP): the CGI-BP. Psychiatry Res 1997; 73:159-171.

NR703 Wednesday, May 24, 12:00 PM - 2:00 PM

Lipid Profiles of Youths Treated With Antipsychotics: A Retrospective Cross-Sectional Evaluation

Monica Leckinger *Cincinnati, OH*, Nick C. Patel, Ph.D., Mary Matias-Akthar, M.D., Michael T. Sorter, M.D., Drew H. Barzman, M.D., Stephen M. Strakowski, M.D., Melissa P. DelBello, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand the potential effects of antipsychotic polypharmacy versus monotherapy on lipid profiles of youths, as well as the effects of specific atypical antipsychotic monotherapy. Also, the participant should be able to recognize the prevalence for specific lipid abnormalities among children and adolescents receiving antipsychotics.

Summary:

Objective: As antipsychotic polypharmacy may be used in children and adolescents with psychiatric disorders, it is important to determine if this treatment approach is associated with a greater risk for dyslipidemia compared to monotherapy.

Method: Medical records of children and adolescents (5 to 18 years) who were treated with at least one atypical antipsychotic during an inpatient psychiatric hospitalization between July 1, 2004 and June 31, 2005, and who had a fasting lipid panel completed while receiving an atypical antipsychotic(s) were reviewed. Total cholesterol (TC), low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglyceride (TG) levels of patients on antipsychotic monotherapy versus polypharmacy were compared. Lipid profiles of patients on aripiprazole, quetiapine, or risperidone monotherapy were also compared. The prevalence of abnormal lipid profiles was determined using accepted criteria.

Results: Sixty-nine patients on antipsychotic monotherapy and 26 on polypharmacy were evaluated. No significant between-group differences in adjusted mean TC, LDL, HDL, and TG levels were observed. There were no significant differences in lipid profiles between patients on aripiprazole, quetiapine, or risperidone. Fifty-one percent and 48% of the total sample were classified as having elevated TG levels and low HDL levels, respectively. The combination of increased TG and decreased HDL was observed in 37% of the total sample.

Conclusions: Fasting lipid profiles of children and adolescents receiving antipsychotic polypharmacy may be similar to those of youths receiving monotherapy. Youths receiving atypical antipsychotics may be at increased risk of elevated TG and/or low HDL levels, and interventions to address these lipid abnormalities may be required. Additional studies are needed to determine if specific antipsychotic regimens are more likely to be associated with dyslipidemia in children and adolescents.

Acknowledgements: This study was supported in part by a NIMH grant MH63373 (MPD).

References:

1. National Cholesterol Education Program Coordinating Committee: Report of the Expert Panel on Blood Cholesterol in Children and Adolescents. Bethesda, MD, National Heart, Lung, and Blood Institute, NIH publication no. 91-2732, 1991.

2. Cook S, Weitzman M, Auinger P, Nguyen M, Dietz WH: Prevalence of a metabolic syndrome phenotype in adolescents: findings from the third National Health and Nutrition Examination Survey, 1988-1994. Arch Pediatr Adolesc Med 2003; 157:821-827.

NR704 Wednesday, May 24, 12:00 PM - 2:00 PM

A Retrospective Claims Analysis of Polypharmacy in the Treatment of ADHD in Adults

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Educational Objectives:

At the conclusion of the presentation, the participant will be aware of the level of polypharmacy associated with various treatments for adult ADHD. They will be aware of treatment practices of colleagues, and they will be aware of various predictors associated with polypharmacy. One predictor highlighted in the abstract is recent care from a psychiatrist. The higher polypharmacy rates seen in this group suggest a difference in patient type/disease severity or, perhaps, a difference in practice patterns.

Summary:

Objective: To quantify the use and investigate factors predicting concomitant medications in the treatment of adult ADHD.

Methods: Data were drawn from a national medical and pharmacy claims database representing more than 80 managed care plans. Patients (18,609) were 18 or older with a diagnosis of ADHD, a claim for ADHD medication during the study period July 2003 to June 2004, and continuous enrollment six months prior to and throughout the study period. Patient-level claims were assigned to calendar months, and months with combined use among the following classes were identified: atomoxetine (ATX), long-acting stimulants (LAS), intermediate-acting stimulants (IAS), short-acting stimulants (SAS), buproprion (BUP), and alpha-2 agonists (A2A). To focus on long-term polypharmacy rather than on transitional management, the first month of each treatment episode was excluded. The effect of prior care from a psychiatrist was investigated via logistic regression within a generalized estimating equations setting. This permitted adjustment for correlation within months recorded for the same patient.

Results: Combination months comprised 19.7% of non-first months for ATX, 21.0% for LAS, 27.4% for IAS, 23.1% for SAS, 36.9% for BUP, and 53.0% for A2A. 4,609 patients had a claim indicating care from a psychiatrist in the six months prior to the study period, and 13,783 did not. Combination months represented 20.5% of the 29,964 months of treatment in patients with prior psychiatric care and 13.6% of 62,756 months of treatment in patients without, odds ratio=1.88 (1.74-2.03).

Conclusion: Greater polypharmacy is evident in adult patients with a history of recent care from a psychiatrist. This may indicate higher burden of disease or greater comfort with polypharmacy among specialists. Eli Lilly and Company funded the research.

References:

1. Wilens TE, Spencer TJ, Biederman J.: A review of the pharmacotherapy of adults with attention-deficit/hyperactivity disorder. J Atten Disord. Mar 2002; 5(4):189-202.

2. Faraone SV, Spencer TJ, Montano CB, Biederman J.: Attention-deficit/hyperactivity disorder in adults: a survey of current practice in psychiatry and primary care. Arch Intern Med. Jun 14 2004; 164(11):1221-1226.

NR705 Wednesday, May 24, 12:00 PM - 2:00 PM

A Flexible Dose, Progressive Titration, Placebo Controlled Trial of Duloxetine for Improving Patient-Reported Functional Outcomes in Adults With GAD

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Educational Objectives:

At the end of this presentation, participants will be knowledgeable that duloxetine is an effective treatment for improving the quality of life and well-being of patients with generalized anxiety disorder.

Summary:

Objective: Across epidemiological and clinical studies, GAD has consistently been associated with diminished well-being, poorer emotional and physical health, and impaired role functioning[1]. The present study examined the efficacy of duloxetine, a balanced and potent reuptake-inhibitor of both 5HT and norepinephrine neurotransmission[2], for improving functional outcomes in adults with GAD. *Methods*: In a double-blind, flexible-dose, progressive-titration trial, 327 patients with a DSM-IV defined GAD diagnosis were randomized; 219 completed 10-week treatment with duloxetine (DLX, N=100) or placebo (PBO, N=119). The primary patient-rated functional outcome measure was the Sheehan Disability Scale (SDS). Quality of Life Enjoyment and Satisfaction Questionnaire Short Form (Q-LES-Q-SF) and EuroQoL-5D were secondary measures administered at baseline and week 10. *Results:* Compared with PBO, patients who received DLX showed significantly greater improvement in SDS Global Functional Impairment scores (Mean change DLX=5.85 versus PBO=3.22, P<.01) and in each of the three SDS domains (work, social life, and family/ home responsibilities) (P<.05). Per protocol-specified analyses, the DLX group (completers) showed greater improvement in Q-LES-Q-SF total and EuroQol-5D index scores compared with PBO group (P<.01). *Conclusions*: In this study, duloxetine was an effective treatment that reduced the disability associated with GAD and enhanced patients' overall functioning and well-being.

References:

1. Mendowitz MV, Stein MB Quality of life in individuals with anxiety disorders. Am J Psychiatry 2000: 157 (5): 669-82.
2. Bymaster FP, Dreshfield-Ahmad LJ, Threlkeld PG, Shaw JL, Thompson L, Nelson DL,. Hemrick-Luecke SK, Wong DT: Comparative affinity of duloxetine and venlafaxine for serotonin and norepinephrine transporters in vitro and in vivo, human serotonin recept.

NR706 Wednesday, May 24, 12:00 PM - 2:00 PM

Quality of Life Measurements in Adult ADHD and Response to Treatment With Mixed Amphetamine Salts Extended Release

Declan Quinn, M.B. *Child and Youth Services, Child Psychiatry, Royal University Hospital, University of Saskatchewan, 241 Ellis Hall, 103 Hospital Drive, Saskatoon, SK, S7N OW8, Canada*

Educational Objectives:

At the conclusion of this session, participants should be able to describe changes in quality of life reported in adults with attention-deficit/hyperactivity disorder given up to 10 weeks of therapy with mixed amphetamine salts extended release 10-60 mg/d.

Summary:

Introduction: Adults with ADHD experience greater quality-of-life (QOL) impairments than non-ADHD peers, with increased psychiatric comorbidity, lower occupational status, and compromised social functioning. QOL improvements in adults receiving ADHD treatment are not well characterized. Traditional evaluation measures focus on efficacy and safety, ignoring QOL.

Methods: This 10-week interim analysis of 36-item Short Form version 2 (SF-36v2) data was conducted as part of the 30-week, open-label, multisite Quality of Life, Effectiveness, Safety, and Tolerability (Qu.E.S.T.) trial in adults (>18 years) with ADHD in community practice settings given once-daily mixed amphetamine salts extended release (MAS XR) 10-60 mg/d. Average scores for the 8 SF-36v2 domains and SF-36v2 mental and physical summary scores were compared with 1998 SF-36 US normative data.

Results: In adults with ADHD (N=702), average baseline SF-36v2 scores for mental health (60.7), social functioning (71.0), role-emotional (64.9), and vitality (46.3) were below US norms. The mental component summary score (39.5) was 1 standard deviation below the 1998 US norm (50.0). Average baseline scores for physical functioning (90.8), role-physical (81.2), bodily pain (80.2), and general health (75.7) were comparable to US norms. The physical component summary score (56.5) was comparable to the 1998 US norm (50.0). With up to 10 weeks of MAS XR 10-60 mg/d, SF-36v2 scores significantly improved for the mental health components (mental health, 73.8; social functioning, 84.5; role-emotional, 83.0; vitality, 63.8), with mean scores at or near US averages and mental component summary score (48.5) comparable to the US norm. Physical component domain scores and summary score (55.9) remained similar to normative levels at baseline.

Conclusions: Adults with untreated ADHD exhibited decreased QOL measures before study initiation, compared with normal US adults. After 10 weeks of MAS XR therapy, QOL scores on the SF-36v2 returned to normal.

This study was funded by Shire Pharmaceuticals Inc.

References:

1. Mannuzza S, Klein RG. Long-term prognosis in attention-deficit/hyperactivity disorder.
2. Klassen AF, Miller A, Fine S. Health-related quality of life in children and adolescents who have a diagnosis of attention-deficit/hyperactivity disorder. Pediatrics.2004;114:e541-547.

NR707 Wednesday, May 24, 12:00 PM - 2:00 PM

GAD in Primary Care Patients: Association Between Severity of Anxiety Symptoms and Health-Related Quality of Life

Dennis A. Revicki, Ph.D. *MEDTAP International, 7101 Wisconsin Avenue, Suite 600, Bethesda, MD, 20814*, Louis Matza, Ph.D., Nancy Brandenburg, Ph.D., Mark Hornbrook, Ph.D.

Educational Objectives:

This presentation will improve participants' understanding of the impact of symptom severity on health-related quality of life (HRQL) in primary care patients with GAD.

Summary:

Objective: GAD is prevalent in primary care settings and significantly impacts patient HRQL. This study evaluated the effect of anxiety symptom severity on HRQL of primary care patients with GAD. **Methods:** Patients ≥18 years old with *DSM-IV*-diagnosed GAD were recruited from the membership of an integrated healthcare delivery system. All patients signed informed consent and agreed to participate in a 6-month longitudinal study. Clinical

assessments included Hamilton Anxiety Rating Scale (HAM-A); HRQL was assessed using Quality of Life Enjoyment and Satisfaction Questionnaire-Short Form (Q-LES-Q-SF), Sheehan Disability Scale (SDS), and SF-12 mental component summary (MCS) and physical component summary (PCS). **Results:** A total of 132 patients were enrolled. Mean age was 47.5±13.9 years; 78% were women. Mean baseline HAM-A score was 16.8±7.6, suggesting moderate anxiety symptoms; mean Q-LES-Q-SF was 46.2±8.7; and mean SDS was 12.9±7.6. Mean baseline PCS and MCS scores of 44.4±9.9 and 44.4±7.3, respectively, were about 0.5 SD units lower than that of the US normative population. At baseline, HAM-A scores were correlated -0.29 ($P<.001$) with MCS; -0.43 ($P<.001$) with PCS; -0.57 ($P<.001$) with Q-LES-Q-SF; and 0.36 ($P<.001$) with SDS. **Conclusion:** Anxiety symptoms reported by GAD patients were significantly associated with increased impairment in HRQL.

References:

1. Kessler RC, Wittchen HU. Patterns and correlates of generalized anxiety disorder in community samples. J Clin Psychiatry. 2002; 63(suppl 8):4-10.
2. Mendlowicz MV, Stein MB. Quality of life in individuals with anxiety disorders. Am J Psychiatry. 2000;157(5):669-682.

NR708 Wednesday, May 24, 12:00 PM - 2:00 PM

Pharmacogenetic Testing of CYP2D6 May Predict EPS With Aripiprazole

Kristen K. Reynolds, Ph.D. *Pharmacogenetics Diagnostic Laboratory, University of Louisville, Pathology and Laboratory Medicine, 511 S. Floyd Street, MDR Room 204, Louisville, KY, 40202,* Anton Surja, M.D., Rif S. El-Mallakh, M.D., Roland Valdes, Jr., Ph.D., Mark W. Linder, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to:

Recognize several cases of aripiprazole-induced EPS in children and adolescents.

Recognize that individual differences in CYP2D6 are important in the efficacy and tolerability of second-generation antipsychotics in general, and aripiprazole in particular

Develop an awareness of the importance of pharmacogenetic testing as a powerful tool to predict adverse drug reactions.

Incorporate pharmacogenetic considerations into medication selection and dosing.

Summary:

Background: Aripiprazole is a new antipsychotic medication that has the unique mechanism of partial agonism at the dopamine D2 receptor. Because of this agonist effect, extrapyramidal reactions (EPS) other than akathisia are quite rare. We observed several cases of children who developed EPS following aripiprazole administration. Aripiprazole is metabolized by the polymorphic Cytochrome P450-2D6 (CYP2D6) enzyme. Individuals with a genetic deficiency of CYP2D6 (poor metabolizers, PMs) have an 80% increase in aripiprazole exposure and twice the elimination half-life compared to subjects with normal CYP2D6 activity (extensive metabolizers, EMs). The consequence of the PM phenotype is increased risk of adverse drug reactions at standard doses of CYP2D6 substrates. This data together with increasing numbers of reports indicating the clinical utility of pharmacogenetic testing led us to examine the CYP2D6 genotype of these patients. *Objective:* To determine whether genetic deficiency of CYP2D6 contributed to increased aripiprazole exposure and development of EPS in these children. *Methods:* Four consecutive children who developed EPS within 1 week of either dose titration or initial aripiprazole administration at standard doses were genotyped. The children (1 female, 3 male) aged 6-15 years, exhibited a variety of EPS including drooling, stiffness, tongue protrusion, cogwheeling, rigidity, Parkinsonism, and NMS-like reactions. These patients were not taking other medications known to interact with aripiprazole. CYP2D6 genotyping was performed in a CLIA-certified clinical laboratory using genomic DNA extracted from patient buccal swabs. *Results:* Two children who developed EPS were found to be CYP2D6 poor metabolizers (no active gene copies), while the other two children were intermediate metabolizers (one active gene copy). *Conclusion:* All of the children who developed EPS following aripiprazole administration were found to have a dysfunctional CYP2D6 enzyme. Pharmacogenetic testing for CYP2D6 may be useful in predicting which patients are at increased risk of aripiprazole-induced adverse drug reactions.

References:

1. Abilify (aripiprazole) prescribing information. Princeton, NJ, Bristol-Myers Squibb Company, 2005.
2. Swainston Harrison T, Perry CM: Aripiprazole: a review of its use in schizophrenia and schizoaffective disorder. Drugs 2004; 64:1715-36.

NR709 Wednesday, May 24, 12:00 PM - 2:00 PM

The Efficacy and Safety of Duloxetine in the Treatment of GAD: A Flexible Dose, Progressive Titration Placebo Controlled Trial

Moira A. Rynn, M.D. *University of Pennsylvania, Mood and Anxiety Disorders Program & CAReS, 3535 Market Street, Suite 670, Philadelphia, PA, 19104-3309,* James Russell, M.D., Janelle Erickson, Ph.D., Michael J. Detke, M.D., Susan G. Ball, Ph.D., Karl Rickels, M.D., Joel Raskin, M.D.

Educational Objectives:

At the end of this presentation, participants will have knowledge about the efficacy and safety of duloxetine as a pharmacological treatment for generalized anxiety disorder.

Summary:

Objective: GAD, a highly prevalent, chronic illness, is associated with dysregulation in serotonergic and noradrenergic neurotransmission[1]. This study examined the efficacy and safety of duloxetine, a balanced and potent dual reuptake-inhibitor of 5HT and norepinephrine,[2] for treatment of GAD. *Methods:* In a 10-week, double-blind, flexible-dose, progressive-titration trial, 327 patients [mean age=41.6 yrs; 61.8% female] with a DSM-IV defined GAD diagnosis were randomized to receive either duloxetine 60 to 120 mg/day (DLX, N=168) or placebo (PBO, N=159). The primary efficacy measure was change from baseline in Hamilton Anxiety Scale (HAM-A) total score; secondary measures included response rates (≥50% HAM-A reduction) and Clinical Global Impression Improvement (CGI-I) scores. *Results:* Compared with PBO, the DLX group demonstrated significantly greater reduction in HAM-A scores (Mean decrease DLX=8.27 versus PBO=6.49, P=.02), greater response rates (DLX=42% versus PBO=30%, P=.03), and greater CGI-I scores (DLX=2.65 versus PBO=2.94, P<.05). Serious adverse events (SAEs) did not differ between groups; the discontinuation rate due to AEs was 20.2% for DLX and 8.2% for PBO (P=.02). The AEs most commonly associated with DLX were dizziness, nausea, and somnolence. *Conclusions:* Duloxetine is an effective, safe treatment for GAD resulting in clinically significant improvement in symptom severity and overall impairment.

References:

1. Connor,KM; Davidson, JRT. Generalized anxiety disorder: Neurobiological and pharmacotherapeutic perspectives. Biological Psychiatry. 1998: 44(12): 1286-1294.

2. Bymaster FP, Dreshfield-Ahmad LJ, Threlkeld PG, Shaw JL, Thompson L, Nelson DL,. Hemrick-Luecke SK, Wong DT: Comparative affinity of duloxetine and venlafaxine for serotonin and norepinephrine transporters in vitro and in vivo, human serotonin recept.

NR710 Wednesday, May 24, 12:00 PM - 2:00 PM

A Pilot Study of the Safety and Effectiveness for Divalproex ER in Pediatric Bipolar Disorder

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Educational Objectives:

To be aware of effectiveness information and side-effect differences between divalproex CD and ER

Summary:

Introduction: Extended release preparations of medications hold promise of decreased side-effects (due to peaks) and better symptom control (decreased troughs). Treatment adherence can also be improved by making treatment regimens simpler. Divalproex (DVP) is available in an extended release preparation that should allow for once a day dosing. *Methods:* Male and female patients ages 7-17 years with a diagnosis of Bipolar I or II Disorder, with or without ADHD, who were clinically very stable (YMRS > 10), on divalproex DR, were offered an 8-week trial of conversion to DVPER. The change could be made for two reasons. First, for persistent side-effects and second for convenience of use. Eighteen subjects were enrolled, 12 had evaluable data. Aims: 1. To determine if package insert guidelines were acceptable for transitioning patients from DVP DR to Extended Release was reasonable for youth with Bipolar Disorder. 2. To determine if side-effects decreased with the conversion due to less peaks. *Results:* Conversion to DVPER from DR was safe and demonstrated improvement in side-effects and in clinical symptoms. SEFCA measures of side-effects were halved. Valproic acid blood levels on the average increased a non-significant amount. Hair loss and gastrointestinal distress were the most common side-effects noted for conversion. These both significantly improved with (pt.05).Transient treatment emergent side-effects were noted. These included increased appetite (25%), somnolence, headache, lethargy and nausea (16%), abdominal pain, dry mouth, epistaxis, joint aches, loose stools and vomiting (8%). In addition, there was some transient exacerbation of mood symptoms in some patients. By the end of the 8 week trial these were decreased to levels below those at baseline. *Conclusions:* The conversion algorithm that takes into account the lower bioavailability of DVPER resulted in a safe transition that consistently resulted in symptom improvement, decreased side-effects, improved patient satisfaction and relatively stable VPA trough levels.

References:

1. Dutta S. Zhang Y. Bioavailability of divalproex extended-release formulation relative to the divalproex delayed-release formulation. Biopharmaceutics & Drug Disposition. 25(8):345-52, 2004 Nov.
2. Kernitsky L. O'Hara KA. Jiang P. Pellock JM. Extended-release divalproex in child and adolescent outpatients with epilepsy. Epilepsia. 46(3):440-3, 2005 Mar.

NR711 Wednesday, May 24, 12:00 PM - 2:00 PM

Types of Sex-Role Identity in Adolescents and Its Relation to Anxiety, Depression, and Suicidal Ideation

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Educational Objectives:

Adolescent is crucial to be competent adult. And the establishment of identity would play a important role in this period. The identity includes many factors, such as self-esteem, body image and sex-role identity, and so on. The oriental way to rear is different from western 's. Thus it could be different patterns to accomplish the sex-role identity between orient and west. At the conclusion of this presentation, the participant should be able to recognize these differences.

Types of sex-role identity in South Korean adolescents and its relation to anxiety, depression and suicidal ideation

Purpose: This study was designed to identify the types of sex-role identity(SRI) in adolescents and to investigate the relation the types of Sustained Release I to depression, anxiety, and suicidal ideation.

Method: Participants were 1,682 high school students(male 591, female 1079) in an urban city. Korean Sex-role inventory, DISC-MDD-SQ, BAI for and Suicidal Ideation Questionnaire-JR was used.

Results: The undifferentiated type(male 67.0%, female (67.3%) was most common, and the next rank was masculine type(male 18.3%, female 17.1%), and androgynous type(male 10.6%, female 8.6%). And feminine type(male 4.2%, female 7.6%) was least, which was statistically significant. The mean score of depression was 10.22(¡¾4.40), and the suicidal ideation mean score was 28.96(¡¾14.53). But the mean score of anxiety was 13.21(¡¾10.38), and there was a significant difference in the level of anxiety on type of Sustained Release I. Especially masculine type had a significant higher anxiety level than undifferentiated type. The level of depression was correlated positively to suicidal ideation.

Conclusion: Disharmony between physical and psychological development has a potential risk for psychological distress, like a depression and anxiety, delinquency, substance abuse, and school-related problem. Also, regarding the sexual identity is the one of the important psychological task in adolescent, balanced education planning is needed to promote to differentiate the sexual role identity in this period.

References:

1. Bem, SL: The measurement of psychological androgyny. J Consult Clin Psychol 1974; 42: 155-162.
2. Bailey JK, Bechtold KT, Berenbaum SA: Who are tomboys and why should we study them?. Arch Sex Behav, 2002; 31(4): 333-341.

NR712 Wednesday, May 24, 12:00 PM - 2:00 PM

Polymorphism of Serotonin Transporter Gene (5-HTTLPR) and Dopamine Transporter Gene (DAT1) in the Two Subtypes of Social Phobia Patients

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand that there are no differences in serotonin and dopamine transporter genotypic distribution between the two social phobia patient groups.

Summary:

Objective

It is suggested that 5HT and dopamine systems play an important role in anxiety disorders, including social phobia. We compared polymorphism of 5HT transporter gene and dopamine transporter gene between the two subtypes, generalized and non-generalized types, of Korean social phobia patients.

Method

Fifty patients diagnosed with social phobia by DSM-IV criterion were included in this study. They were divided into two subtypes, generalized and non-generalized types. Twenty-one were generalized type and 29 were non-generalized type. Five milliliters of blood was taken from each patient and genomic DNA was extracted from the white blood cell. PCR analyses were done. For comparing the distribution of 5HT transporter gene and dopamine transporter gene between the two groups, Pearson Chi-Square test was used. All of the analyses were performed using standard software (SPSS for Windows), and p values of less than 0.05 were considered statistically significant.

Results

We found 3 genotypes (5-HTTLPR ss, ls, ll) of 5HT transporter, and 4 genotypes (DAT110/10, 7/10, 9/10, 10/11) of dopamine transporter. There were no significant differences in 5HT transporter ($\chi 2$=2.16, p=0.33) and dopamine transporter ($\chi 2$=2.89, p= 0.40) genotypic distribution between the two subtypes of Korean social phobia patients.

Conclusions

There were no significant differences in 5HT transporter and dopamine transporter genotypic distribution between the two social phobia patient groups. However, the sample size was small and more subjects should be recruited in further study.

References:

1. Dan J. Stein: Social Anxiety Disorder and General Anxiety Disorder: Serotonergic and Dopaminergic Neurocircuitry. J Clin Psychiatry 2002;63[suppl 6]:12-19.
2. Westenberg HG: The nature of social anxiety disorder. J Clin Psychiatry 1998;59[suppl 17]:20-26.

NR713 Wednesday, May 24, 12:00 PM - 2:00 PM

Extended-Release Dexmethylphenidate in ADHD: Efficacy in Children of Different Racial and Ethnic Backgrounds

Raul R. Silva, M.D. *NYU School of Medicine, 550 First Avenue, NB21 South 6, New York, NY, 10016*, Ann Childress, M.D., Frank A. Lopez, M.D., Matthew Brams, M.D., Linda Pestreich, B.S.C., Jim Wang, Ph.D., Rafael Muniz, M.D.

Educational Objectives:

Some evidence suggests racial/ethnic differences in ADHD symptoms, but little is known about responses to pharmacotherapy in different patient groups. At the conclusion of this presentation, the participant should be able to:

ummarize the effects of d-MPH-ER in children of different races and ethnicities.

Describe the scope and time course of responses to d-MPH-ER over 12 hours postdose.

Summary:

Introduction: Racial/ethnic groups may differ in their responses to pharmacotherapy for ADHD. This analysis assessed the efficacy of extended-release dexmethylphenidate (d-MPH-ER) in children of different racial and ethnic backgrounds.

Methods: Results were pooled from two randomized, multicenter, double-blind, crossover studies comparing 20 mg d-MPH-ER versus placebo in children 6-12 years old with ADHD in a laboratory classroom over 12 hours postdose. Efficacy variables included SKAMP-Combined, -Attention, and -Deportment scores; and math problems attempted and correctly answered.

Results: The pooled analysis included 67 "White," 22 "Black," and 32 "Hispanic/Other" patients. For all groups, d-MPH-ER was associated with sustained improvement from predose on all efficacy measures, whereas placebo was associated with worsening from predose. Over the entire 12-hour assessment period, the advantages of d-MPH-ER over placebo were generally similar for the White, Black and Hispanic/Other children. For SKAMP scores, AUC_{0-12} values showed that the improvements during d-MPH-ER treatment were evident across ethnic groups, although the difference between White patients (-66) and Black patients (-53) in SKAMP-Attention scores reached borderline statistical significance (*P*=0.0575). SKAMP score worsening during placebo treatment tended to be somewhat greater in the Hispanic/Other group than in the other ethnic groups. The trend toward larger deterioration during placebo treatment in Hispanic/Other children was most pronounced in the morning and early afternoon, as shown by AUC_{0-4} and AUC_{4-8} values.

Conclusions: Results from this post-hoc, pooled analysis suggest that the efficacy of d-MPH-ER is generally consistent, but some differences exist across White, Black, and Hispanic/Other groups. In a laboratory classroom setting, improvements in attention, behavior, and productivity are seen regardless of race or ethnicity. In untreated patients, the daily course of ADHD symptoms may vary across racial or ethnic groups.

References:

1. Silva RR, Muniz R Pestreich L: Exploratory Analysis of Race/Ethnicity and Response to Methylphenidate. Scientific Proceedings from the American Academy of Child and Adolescent Psychiatry 51st Annual Meeting., Washington, D.C. October 19-24, 2004, pg.
2. Epstein JN, Willoughby M, Valencia EY, et al. The role of children's ethnicity in the relationship between teacher ratings of attention-deficit/hyperactivity disorder and observed classroom behavior. J Consult Clin Psychol. 2005;73:424-434.

NR714 Wednesday, May 24, 12:00 PM - 2:00 PM

The Relationship Between the Strengths and Difficulties Questionnaire Scores and the Child Behavior Checklist Scores: Korean Rural Community

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to confirm the usefulness of the Strengths and Difficulties Questionnaire(SDQ) as a screening measure about the psychiatric and behavioral problems of the children in Korean rural community, according to the investigation of the relationship between the SDQ scores and the Child Behavior Checklist(CBCL) scores.

Summary:

Objectives ;

This study was to explore the usefulness of the Strengths and Difficulties Questionnaire(SDQ) in Korean rural community, investigating the relationship between the SDQ scores and the Child Behavior Checklist(CBCL) scores.

Methods ;

The SDQ and CBCL were administered to 323 parents of elementary school children in Cheong-won province, one of the rural area in Korea. The relationship between the results of each mea-

sure were tested using Pearson correlation coefficients. Stepwise regression analysis was also performed.

Results ;

1) Each scores of four scales(emotional, conduct, hyperactivity/inattention, peer relationship problems) and the total difficulties scores of SDQ were positively correlated with the scores of many subscales of the Behavioral Problem Scale of CBCL.

2) The scores of the prosocial scale of SDQ were negatively corrlated with the scores of Anxious/Depressed($p<.01$), Social Problems($p<.01$), Attention Problems($p<.01$), and Aggressinve Behavior($p<.01$) subscale of the Behavioral Problem Scale of CBCL.

3) According to the results of stepwise regression analysis, the total difficulties scores of SDQ was explained by the scores of all subscales of the Behavior Problem Scale of CBCL(R^2=21.5%), especially, Total Problems(β=.323) and Delinquent subscale(β =.199).

Conclusion ;

The SDQ is useful for the screening measure for Korean rural children, but the additional use of other measures might be needed.

References:

1. Goodman R: The strengths and difficulties questionnaire: a research note. J Child Psychol Psychiatry 1997; 38: 581-586.
2. Koskelainen M, Sourander A, Kaljonen A: The Strengths and Difficulties Questionnaire among Finnish school-aged children and adolescents. European Child Adolesc Psychiatry 2000; 9: 2777-284.

NR715 Wednesday, May 24, 12:00 PM - 2:00 PM

Pharmacokinetic/Pharmacodynamic Analysis of Hyperactive-Impulsive and Inattentive Symptoms During Atomoxetine Treatment in Children and Adolescents With ADHD

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Educational Objectives:

At the conclusion of this presentation, the participant should be aware that improvements in ADHD symptoms during treatment with atomoxetine are proportional to (A) measured blood-level exposure and (B) administered dose.

Summary:

Objective: To determine the relationship between atomoxetine exposure and improvement in hyperactive/impulsive and inattentive symptoms of ADHD.

Methods: Subjects aged 8-18 with *DSM-IV* ADHD were treated for approximately 8 weeks with atomoxetine under randomized, double-blind, placebo-controlled conditions. Bayesian clearance estimates were obtained from 189 subjects receiving atomoxetine, from which area-under-curve (AUC) exposures were calculated. The relationship between efficacy and exposure was examined using a nonlinear model to fit the observed AUC and changes from baseline in ADHD Rating Scale (ADHDRS-IV-Parent:Inv) total and subscale (Hyperactivity/Impulsivity, Inattention) scores.

Results: The resulting fit indicates an expected maximum possible improvement (E_{max}) from baseline in ADHDRS-IV-Parent:Inv total scores for atomoxetine of -17.4, compared with -6.2 for placebo. Expected maximum improvements from baseline for 0.5-, 1.2-, and 1.8-mg/kg/day doses were equivalent to 62%, 78%, and 85% of E_{max}, respectively. Corresponding maximum improvements for the *Hyperactivity/Impulsivity* subscale for the 3 doses equated to 64%, 79%, and 86% of E_{max}, respectively, while those for the *Inattention* subscale equated to 60%, 78%, and 85%. Conclusion: These results indicate similar relationships between exposure and improvements in the hyperactive/inattentive and inattentive symptoms of ADHD.

References:

1. Farid NA, Bergstrom RF, Ziege EA, Parli CJ, Lemberger L: Single-dose and steady-state pharmacokinetics of tomoxetine in normal subjects. J Clin Pharmacol 1985; 25:296'301.
2. Witcher JW, Long A, Smith B, Sauer JM, Heiligenstein J, Wilens T, Spencer T, Biederman J: Atomoxetine pharmacokinetics in children and adolescents with attention deficit hyperactivity disorder. J Child Adolesc Psychopharmacol 2003; 13:53'63.

NR716 Wednesday, May 24, 12:00 PM - 2:00 PM

A Double Blind, Six-Month Study of Methylphenidate in Adults With ADHD

Thomas J. Spencer, M.D. *Mass General Hospital, 55 Fruit Street. YAW 6, Boston, MA, 02114*, Joseph Biederman, M.D., Timothy E. Wilens, M.D., Robert L. Doyle, M.D., Craig B. Surman, M.D., Eric Mick, D.Sc.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to treat adult ADHD over the medium term.

At the conclusion of this presentation, the participant should be able to describe the medium term tolerability of stimulants in adult ADHD

Summary:

Objective. The current study expands the scope of previous studies of adult ADHD by examining a maintenance phase to assess the magnitude and drug-specificity of medium-term effectiveness over a six month period.

Methods. This was a double-blind, placebo-controlled, parallel study of adult ADHD with three phases. Phase I of the study consisted of a six week controlled study of short term efficacy in which patients were randomized to methylphenidate (MPH). Responders (> 30% decrease in the Adult ADHD Investigator Symptom Report Scale (AISRS)) to Phase I were continued into Phase II and assessed every four weeks for six months under double-blind conditions.

Results. 65 Phase I responders [MPH (N=59) versus placebo (N=6)] were continued under double-blind conditions for another 24 weeks to assess the stability of response over the long-term. During the 24 week follow-up, the mean dose remained within a narrow range for both MPH and placebo (82-87 mg/day [1.0-1.1 mg/kg] and 89-93 mg/day [1.2-1.3 mg/kg] for MPH and placebo respectively, t's < 1.6, p's>0.1) Response of ADHD symptoms continued over the 24 weeks of the study with little change in mean severity of the ADHD symptoms on the AISRS from week 0 to 24 (9.1$\pm$5.6 to 10.7$\pm$8.4 for MPH versus 12$\pm$3.0 to 15.7$\pm$6.8 for placebo) We operationalized worsening of ADHD symptomatology as the loss of the 25% improvement of ADHD symptom severity on the AISRS. Survival analysis revealed an adjusted rate of 15% of subjects on MPH versus 52% on placebo, (C2(1)= 6.5, p=0.01) who had one rating of loss of response over the 24 weeks.

Conclusion MPH was effective and well tolerated in the medium-term treatment of adults with ADHD. Patient satisfaction was improved over six months in multiple domains. Vital signs did not reveal any untoward effects of six months of MPH treatment.

References:

1. Spencer TJ, Biederman J, Wilens T, et al. A large Double Blind Randomized Clinical Trial of methylphenidate in the treatment

of adults with ADHD. Biologic Psychiatry. 2005 Mar 1;57(5):456-63.

2. Kessler R, Adler L, Barkley R, et al. The prevalence and correlates of adult ADHD in the United States: Results from the National Comorbidity Survey Replication, American Journal of Psychiatry. 2005, In Press.

NR717 Wednesday, May 24, 12:00 PM - 2:00 PM

Escitalopram in the Treatment of OCD

Dan J. Stein, M.D. *University of Cape Town, Department of Psychiatry-J Block, Groote Schuur Hospital, Anzio Rd. Observatory 7925, Cape Town, 7925, South Africa*, Brigitte Tonnior, Pharm.D., Elisabeth W. Andersen, Ph.D.

Educational Objectives:

The participants will be able to evaluate the efficacy and tolerability of escitalopram in the treatment of obsessive-compulsive disorder

Summary:

Introduction: The efficacy and tolerability of escitalopram were investigated in a 24-week, randomised, placebo-controlled, active-reference, double-blind study in OCD.

Methods: Adult patients were assigned to treatment with placebo (N=115), escitalopram 10mg/day (N=116), escitalopram 20mg/day (N=116), or paroxetine 40mg/day (N=119) (1,2). The pre-specified, primary efficacy endpoint was the mean change from baseline in Y-BOCS total score at Week 12 (ITT, LOCF) using ANOVA.

Results: After 12 weeks, on the primary efficacy endpoint, there was a statistically significant difference from placebo for 20mg escitalopram and paroxetine. At Week 24, the proportion of remitters (Y-BOCS≤10, LOCF, pre-defined) was significantly ($p<0.05$) greater for 20mg escitalopram (41.2%) than placebo (27.4%), but not for 10mg escitalopram (36.6%) or paroxetine (37.9%). The response rate (≥25 decrease from baseline Y-BOCS, LOCF, pre-defined) was significantly greater than placebo (50.4%) for 20mg escitalopram (70.2%) and paroxetine (67.2%). The incidence of adverse events (AEs) was 64% (placebo), 71% (10mg escitalopram), 75% (20mg escitalopram), and 80% (paroxetine). The three AEs with the highest incidences in the active treatment groups were nausea (19-27%), headache (17-22%) and fatigue (12-19%). AE withdrawal rates were 7.9% (placebo), 8.8% (10mg escitalopram), 11.4% (20mg escitalopram), and 15.4% (paroxetine).

Conclusion: Both 10 and 20mg/day escitalopram were efficacious and well tolerated in the treatment of OCD.

References:

1. Zohar J, Judge R. Paroxetine versus clomipramine in the treatment of obsessive-compulsive disorder. Br J Psychiatry, 1996; 169: 468-474.

2. Hollander E, Allen A, Steiner M, et al. Paroxetine OCD Study Group. Acute and long-term treatment and prevention of relapse of obsessive-compulsive disorder with paroxetine. J Clin Psychiatry. 2003;64: 1113-1121.

NR718 Wednesday, May 24, 12:00 PM - 2:00 PM

Which Factors Predict Placebo Response in Anxiety Disorders and Major Depression?

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Educational Objectives:

The participant will gain knowledge concerning some of the factors that may influence placebo response in anxiety disorders and major depression.

Summary:

Introduction: The placebo response rate has increased in a number of psychiatric disorders, and this response is a major issue in the design and interpretation of clinical trials (1,2). It was therefore the aim of the current investigation to identify potential predictors of placebo-response through examination of the placebo-controlled clinical trial database for escitalopram in MDD and three anxiety disorders.

Methods: All placebo-controlled studies of escitalopram in MDD and in anxiety disorders (GAD [GAD], social anxiety disorder [SAD], panic disorder [PD]) were included. Potential predictors examined were type of disorder, (for example GAD *versus* MDD); location of study (United States *versus* European Union); dosing regime (flexible *versus* fixed); number of treatment arms; gender of subjects; and duration and severity of disorder.

Results: Placebo responses were greater in studies conducted in the European Union, in flexible dose studies in MDD, in less severe anxiety disorders and less severe GP-treated MDD, and in depressive episodes of shorter duration (but not in shorter duration anxiety disorders). In GAD, placebo response rate was higher in trials with a number of the analyzed factors, including EU location, GP setting, flexible dose design, and increased number of treatment arms.**Conclusion**: Additional work is needed before definitive recommendations can be made about whether standard exclusion criteria in clinical trials of antidepressants, such as mild severity of illness, do in fact maximize medication-to-placebo differences. This analysis in a range of anxiety disorders and MDD suggests that there may also be instances where the predictors of placebo response rate themselves vary across different conditions.

References:

1. Piercy, M A, Sramek, J J, Kurtz, N M, and Cutler, N R. Placebo response in anxiety disorders. Ann Pharmacother 1996;30: 1013-1019.

2. Stolk, P, Ten Berg, M J, Hemels, M E, and Einarson, T R. Meta-analysis of placebo rates in major depressive disorder trials. Ann Pharmacother 2003;37: 1891-1899.

NR719 Wednesday, May 24, 12:00 PM - 2:00 PM

Defenses, Defensiveness, Social Desirability and Global Functioning in Normal Adolescents

Hans Steiner, M.D. *Stanford University, 401 Quarry Road, Room 1117, Stanford, CA, 94305*, Sanja Medic, Niranjan S. Karnik

Educational Objectives:

1. To educate the practitioner regarding the role of defenses, defensiveness, social desirability and global functioning in normal adolescents

2. To use the knowledge in the treatment

Summary:

Objective: To examine the relationship of Defenses, Defensiveness, Social Desirability and Global Functioning in adolescents. There are mixed results in the literature concerning the relationship of these variables to adjustment.

Method: We studied 140 high school students in two school districts (mean age 16, SD 1; 53% girls). Global Assessment of Functioning Ratings were applied blindly and independently (correlations between raters 0.89). Subjects completed three standardized self report inventories measuring social desirability (Mar-

low Crowne Social Desirability Scale), Defensiveness (Weinberger Adjustment Scale) and the Response Evaluation Measure - 71), measuring defenses.

Results: Social Desirability, Defensiveness and Immature and Mature Defenses correlated modestly to moderately (Pearson's r ranging from 0.52 to .16; all p's <0.05).

Immature defenses correlated negatively with GAF (-0.31); Mature defenses correlated positively with GAF (r=0.25, all p's <0.05). Neither Social Desirability nor Defensiveness achieved significant results. In a linear regression, controlling for age and gender effects, both sets of defenses contributed significantly (beta = 0.33 and 0.19 respectively), while taking into account defensiveness and social desirability (r squared = 13%; F(7/109)=2.3; p=0.03)

Conclusion:

Classical defense profiles overlap modestly with measures of defensiveness and social desirability. Defense profiles are useful additional tools to assess mental health.

References:

1. Steiner H, Araujo K, Koopman C: The Response Evaluation Measure: A New Instrument for the Assessment of Defenses. Am J Psychiatry 2001; 158(3):467-473.
2. Erickson S, Steiner H: Predicting Adolescent's Global Functioning from Personality Typologies. Child Psychiat Hum D 2003; 34(1): 63-80.

NR720 Wednesday, May 24, 12:00 PM - 2:00 PM

Personality Disorders in Incarcerated Delinquents: Results of a Structured Interview Study (SID-P)

Diana L. Tracy, B.S. *Dayton*, Niranjan S. Karnik, M.D., Marie V. Soller, M.D., Hans Steiner, Dr. Med. Sc.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand that Personality Disorder criteria met by Incarcerated youth occurs at a high rate.

Summary:

Objective: To document personality disorders in incarcerated delinquents. Previous studies report extensive Axis I morbidity in incarcerated youths. This study extends these findings to personality disorders in order to assist systems of care to appropriately address these clinical targets.

Method: After 9-months of incarceration at the California Youth Authority, 790 (10-17 year old) adolescents (650 boys and 140 girls) voluntarily assented to participate. Youths completed the Structured Interview for DSM-IV Personality (SID-P). Although some of these youths were under 18, given the chronicity and severity of their symptoms, a high prevalence of personality disorders, particularly antisocial personality disorder was anticipated.

Results: Antisocial Personality Disorder criteria were met by the majority of subjects with a personality disorder (girls 91%, boys 92%).Almost half of the girls (n=140, 44%) and one-fifth of the boys (n=650, 20%) met DSM-IV criteria for additional personality disorders. Criteria for Schizoid, Schizotypal and Narcissistic Personality Disorder were met in 2-4%, 2% and 8% of subjects, respectively. More girls (41%) than boys (13%) with a personality disorder met criteria for BPD.

Conclusions: Incarcerated adolescents fulfill personality disorders criteria at a very high rate. There is reason to believe that personality disorders contribute significantly to criminal recidivism.

References:

1. Steiner H, Cauffman E, Duxbury E (1999), Personality Traits in Juvenile Delinquents: Relation to Criminal Behavior and Recidivism. J Am Acad Child Adolesc Psychiatry 38:256-262.
2. Bowlby J (1944), Forty-four juvenile thieves: their characters and home-life. Int J Psychoanal 25:1-57.

NR721 Wednesday, May 24, 12:00 PM - 2:00 PM

Safety and Efficacy of Venlafaxine ER in Adolescents With Panic Disorder

Karen A. Tourian, M.D. *Wyeth Research, 500 Arcola Road, Collegeville, PA, 19101-2538*, Anne Marie Albano, Ph.D., Evan Tzanis, John S. March, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to

Discuss the effects of venlafaxine ER on the symptoms of panic disorder (PD) in adolescents, and

Compare the efficacy and safety of venlafaxine ER with placebo in the treatment of PD in adolescents.

Summary:

Objective: To study the safety and efficacy of venlafaxine (Effexor®) Extended Release (extended release) in adolescents with panic disorder (PD).

Method: This 10-week double-blind, placebo-controlled study of venlafaxine Extended Release (flexible dose; range determined by weight) enrolled outpatients aged 12 to 17 years (intent to treat, n=46), who met DSM-IV criteria for PD (± agoraphobia), had ≥4 full-symptom panic attacks within 4 weeks of screening, ≥2 full-symptom panic attacks during screening, and Clinical Global Impression (CGI)-Severity score ≥4. A MDD diagnosis or a Children's Depression Rating Scale score >55 were exclusionary.

Results: Exploratory analyses found no significant differences between groups at any time point on the primary (full-symptom panic attack frequency) or 2 key secondary efficacy variables (Panic Disorder Severity Scale-A total score, and response [CGI-Improvement=1 or 2]). Venlafaxine Extended Release treatment was associated with few clinically important changes in laboratory test results, vital signs, or ECGs. There were no suicides or other indicators of suicidality. There were no deaths in the study, and no serious adverse events in the venlafaxine Extended Release group. No venlafaxine Extended Release -treated patients withdrew because of adverse events.

Conclusions: The adverse events observed with venlafaxine Extended Release in this study were similar to those observed with venlafaxine Extended Release in premarketing studies for MDD, GAD, and generalized social anxiety disorder in adults, children, and adolescents. No patients in the venlafaxine Extended Release treatment group withdrew from the study because of adverse events, indicating that there is no evidence of an increased risk in patients with PD. Physicians should be alert to signs of suicidal ideation in pediatric patients taking venlafaxine Extended Release .

Supported by funding from Wyeth Research.

References:

1. Kunz N, Khan A, Nicolacopoulos E, Jenkins L, Yeung PP: Venlafaxine extended release for the treatment of children and adolescents with generalized anxiety disorder. Int J Neuropsychopharmacol 2002; 5:S160.
2. Tourian K, March J, Mangano R. Venlafaxine ER in children and adolescents with social anxiety disorder [poster]. Presented at American Psychiatric Association Annual Meeting. New York, NY. May 1-6, 2004.

NR722 Wednesday, May 24, 12:00 PM - 2:00 PM

Risperidone Use and Glucose Dysregulation in Children

Atilla Turgay, M.D. *Scarborough Hospital, Psychiatry, 3030 Birchmount Road, Toronto, ON, M5G 2C4, Canada*, Suleyman Atabek, M.D., Selma Ercan, hakan erdogan, M.D., gulseven kilicli, M.D.

Educational Objectives:

At the end of this session the attendants will be able to review the effective strategies for weight control in risperidone use and possible side effects

Summary:

Objective: To study the effects of risperidone use over a 10-month period on blood glucose (fG), HbAic, amylase and lipase levels and to review and monitor weight changes in children.

Method: The open-label study sample consisted of 23 children and adolescents (ages 4.5-17.5 years) who were treated with risperidone for various psychiatric disorders. All subjects were medication free for at least three months prior to the onset of the study and had normal blood values at the baseline for glucose (fG), HbAic, amylase and lipase levels. The blood values for these were measured every other month. The average risperidone dose was 1.55±0.98 mg/day.

Results: During the ten-month study period, there were no clinical symptoms of glucose dysregulation and/or diabetes. The blood values for glucose (fG), HbAic, amylase and lipase levels remained within the normal range and no statistically significant changes were found in these blood values, weight or BMI. There were no cases of discontinuation due to side-effects and/or glucose dysregulations.

Conclusions: Risperidone use at the given dose level was not associated with significant weight gain and/or glucose dysregulation within the ten-month study use. For longer periods of use, regular check-ups should continue in order to monitor weight control and blood values.

References:

1. Turgay A, Binder C, Snyder R, Fisman S. Long term safety and efficacy of risperidone for the treatment of disruptive behavior disorders in children with subaverage IQs; Pediatrics 2002: Vol 100, No. 3 e34.
2. Turgay A, Binder C. Risperidone-associated diabetes mellitus in children. Pediatrics 2004; 2:113.

NR723 Wednesday, May 24, 12:00 PM - 2:00 PM

Developmental Changes in Comorbidity in ADHD

Atilla Turgay, M.D. *Scarborough Hospital, Psychiatry, 3030 Birchmount Road, Toronto, ON, M5G 2C4, Canada*, Rubaba Ansari

Educational Objectives:

At the end of this presentation the attendents will be able to outline the common comorbid disorders associated with ADHD and their impact on treatment

Summary:

Objective: to evaluate the frequency, nature and developmental changes in ADHD comorbidities

Method: This study involved 2902 patients with ADHD, between age 2-82. The final diagnosis was given by a child psychiatrist who reviewed youth, parent, teacher ratings scales of Gadow-Sprafkin Child, Adolescent and Adult Symptom Inventories and DuPaul ADHD Rating Scales. Patients who had 1.5 SD above the mean provided by DuPaul who also met the diagnostic criteria for DSM-IV were included in the study.

Results: ADHD is frequently associated with other comorbid disorders throught the life cycle. In early childhood Oppositional Defiant Disorder (ODD) is very common (Age 2-5: 60.67%), in adults over 19, ODD is found in 4.71% of the patients. Major Depression is very rare in children age 2-16: 2.3% but in adults, most frequent comorbid disorder is Major Depression (41.08%). Anxiety Disorders increase by age. Ony Major Depression and Anxiety Disorders are more common in females ($p<0.001$). Behavior Disorders are more common in males throughout the life cycle ($p<0.001$).

Conclusions: ADHD is commonly associated with different disorders in different developmental stages. Since different comorbid disorders require different treatment approaches, screening for comorbidities with reliable rating scales and structured interviews is essential for effective treatment.

References:

1. Turgay A. Aggression and disruptive behavior disorders in children and adolescents. Expert Rev Neurotherapeutics 2004 4:623-632.
2. Lalonde J, Turgay A, Hudson JI. Attention deficit hyperactivity disorder and comorbid disruptive behavior disorders in a child and adolescent mental health clinic. Can J Psychiatry, 1998, 43:623-628.

NR724 Wednesday, May 24, 12:00 PM - 2:00 PM

Comorbidity in Adolescents With ADHD

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Educational Objectives:

At the end of this session the attendee will be able to describe the major comorbidities in adolescent ADHD

Summary:

Objective: To determine the frequency and nature of comorbid disorders and gender differences in adolescents with ADHD.

Method: The sample consisted of 594 adolescents (447 males, 147 females), aged 13-18 years. Diagnoses were made by a child psychiatrist using clinical interviews, the Gadow-Sprafkin Child Symptom Inventory (youth, parent and teacher versions) and the DuPaul ADHD Rating Scales. Patients with scores 1.5 SD above the mean on the DuPaul Scale and who also met the DSM-IV diagnostic criteria for ADHD were included in the study.

Results: In the present study, there was a higher proportion of males; the M:F ratio of the clinical sample was 3.40:1. Approximately 16 % of the sample had ADHD as a single diagnosis. Oppositional Defiant Disorder: 61.97% versus 60.54%; Conduct Disorder 30.87% versus 27.89%; Anxiety Disorders 14.32% versus 15.65%; Major Depression 10.29% versus 25.17%; Dysthyic Disorder 12.53% versus 17.01%). There were no statistically significant gender differences, with the exception of Major Depression; it was found more commonly in females ($p<0.001$).

Conclusions: ADHD is often highly comorbid with other disorders in adolescents. Comprehensive assessments using thorough clinical histories, ratings scales and structured interviews are necessary to accurately identify individual comorbidity profiles. These will be useful in medication selection and treatment/follow-up.

References:

1. Turgay A. Treatment of comorbidity in conduct disorder with ADHD. Essential psychopharmacology 2005, 6:277-290.
2. Jensen P. Standards of the use of stimulants. Pediatr Child Health 2004, Suppl. 8B-12B.

NR725 Wednesday, May 24, 12:00 PM - 2:00 PM

Adult ADHD: Gender Differences and Comorbidity

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Educational Objectives:

at the end of this session the attendees will be able to list the common adult ADHD comorbid disorders and most effective strategies in treatment

Summary:

Objective: To determine the frequency and nature of comorbid disorders and gender differences in adults with ADHD.

Method: The study sample consisted of 297 adults (210 males, 87 females), ages 19-82 years. Diagnoses were made by a psychiatrist using semi-structured clinical interviews and multiple rating scales (Gadow-Sprafkin-Weiss Adult Symptom Inventory, Derogatis' SCL 90, Turgay Adult ADHD Rating Scale). In cases of Mood or Anxiety Disorders, the Hamilton Depression and Hamilton Anxiety Disorder Rating Scales were utilized.

Results: The proportion of males was significantly higher than females; the M:F ratio of the clinical sample was 2.41:1. Approximately 32.3% of the sample had ADHD as a single diagnosis. The M:F ratios for major comorbid disorders were as follows: Major Depression: 35.71% versus 54.02%, Anxiety Disorders: 14.76% versus 18.52%, Dysthymic Disorder: 12.86% versus 16.09%, Oppositional Defiant Disorder: 5.24% versus 3.45% and Conduct Disorder: 0.48% versus 3.45%/. There were no statistically significant gender differences, with the exception of Major Depression (p=0.01942) and Anxiety Disorders (p=0.02506); they were more prevalent in the female sample.

Conclusions: ADHD has a high rate of comorbidity in adults. Clinicians must do thorough assessments using comprehensive structured interviews and ratings scales to determine individual comorbidity profiles. This is imperative in the selection of treatment and/or medications and the follow-up monitoring.

References:

1. Gadow K, Sprafkin J. Child Symptom Inventory, Checkmate Plus, 1987, NY, USA.
2. Yildiz A, Sachs GS, Turgay A,. Pharmacological management of agitation in emergency settings. Emerg Med J. 2003; 20:339-346.

NR726 Wednesday, May 24, 12:00 PM - 2:00 PM

Parent-Rated Effects of Transdermal Methylphenidate in Children With ADHD

John Turnbow, M.D. *Westex Clinical Investigations, 3315 81st St Suite A, Lubbock, TX, 79423*, Sharon B. Wigal, Ph.D., Howard Abikoff, Ph.D., James J. McGough, M.D., Daniel Sea

Educational Objectives:

At the conclusion of this presentation, the participant should be able to:

Describe the clinical use of the methylphenidate transdermal system (MTS) in pediatric subjects.

Discuss parent-based ratings of efficacy and behavior as compared to placebo in the home environment.

Summary:

Objective: Assess the efficacy of a methylphenidate transdermal system (MTS) compared to a placebo transdermal system (PTS) in a laboratory classroom setting.

Method: This was a randomized, double-blind, placebo-controlled, laboratory classroom, crossover study with a 5-week open-label dose optimization phase. Children aged 6-12 years diagnosed with ADHD by DSM-IV-TR criteria were enrolled. Measures of efficacy included the Conners' Parent Rating Scale-Revised: Short Form (CPRS-R), completed at 11:00am and 3:00pm on the last weekend day prior to all study site visits. Subscales for ADHD index, oppositional, hyperactivity, and cognitive problems were used to assess behavior.

Results: Mean CPRS-R total scores for MTS treatment were significantly lower compared to placebo overall [20.2 ($\pm$2.11) versus 35.3 ($\pm$2.21), respectively; p<0.0001], and at the 11:00am (p<0.0001) and 3:00pm (p<0.0001) time points. Overall mean scores for MTS treatment were significantly lower compared to placebo for the ADHD index (p<0.0001), oppositional (p<0.0001), hyperactivity (p<0.0001), and cognitive problems (p<0.0001) subscales.

Conclusion: Treatment with MTS resulted in statistically significant improvements in behavior compared with placebo on parent assessments. MTS was generally well-tolerated, and there were no serious adverse events. MTS may be an effective non-oral alternative treatment for ADHD in pediatric subjects.

Supported by funding from Shire US Inc.

References:

1. Conners CK. Conners' Rating Scales-Revised: Technical Manual. New York, Multi-Health Systems, Inc., 1997.
2. Wigal S, McGough JJ, Abikoff H, Turnbow J, Posner K, and Moon E. Behavioral effects of methylphenidate transdermal system in children with ADHD. Poster presented at the joint meeting of AACAP and CACAP. Toronto, Ontario. October 21, 2005.

NR727 Wednesday, May 24, 12:00 PM - 2:00 PM

A Randomized Control Trial of Olanzapine in the Treatment of Trichotillomania

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to:

1. understand the potential benefit of olanzapine in the treatment of trichotillomania.

2. understand where Trichotillomania fits on the Obsessive Compulsive Disorder Spectrum.

Summary:

Objective: Trichotillomania (TTM) or hair-pulling has been considered as part of the obsessive compulsive disorder (OCD) spectrum. TTM treatment with OCD medications has largely been unsuccessful. Tics/Tourrettes' Syndrome (TS), another OCD spectrum disorder that is also unresponsive to SSRIs (SRI's), has a clinical phenomenology like TTM. We hypothesized that treatments for TS may work in TTM.

Method: Twenty-three patients with DSM-IV TTM were randomly assigned to a 12 week trial of olanzapine or placebo. Medication was started at 2.5 mg/day and increased to a maximum dose of 20 mg/day.

Results: Preliminary interim analysis revealed that 10 of 23 (43.5%) patients, were considered responders by Clinical Global Impression-Improvement Scale (CGI-I). There was a significant change from baseline to endpoint in the Yale-Brown Obsessive Compulsive Scale for TTM ($p \leq .01$), the Massachusetts General Hospital Hair Pulling Scale ($p \leq .05$) and CGI-Severity ($p \leq .01$). Mean dose at endpoint was 14.3 $\pm$ 6.3 mg/day. Nineteen of 23

patients (82.6%) reported at least one adverse event, but none resulted in early withdrawal from the study.

Conclusion: There was significant improvement in TTM symptom measures from baseline to endpoint. TTM symptom response and overall response rates will be discussed by treatment group.

References:

1. Van Ameringen M, Mancini C, Oakman JM, Farvolden P: The potential role of haloperidol in the treatment of trichotillomania. Journal of Affective Disorders 1999; 56:219-226.
2. Lochner C, Seedat S, duToit PL, et al: Obsessive-compulsive disorder and trichotillomania: a phenomenological comparison. BMC Psychiatry 2005; 5(1):2.

NR728 Wednesday, May 24, 12:00 PM - 2:00 PM

Symptom Relapse Following Switch From Celexa to Generic Citalopram in an Anxiety Disorders Clinic Case Series

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to:

1. become aware of potential differences in clinical effect between generic and brand name citalopram.

2. examine potential risks posed by a switch from brand name to generic citalopram in an anxiety disorders case series.

Summary:

Objective: Generic agents do not require large clinical trials of safety and efficacy required by their brand name counterparts, although they are required to demonstrate both pharmacological and bio-equivalence. Bioequivalence is attained when the extent of absorption of the generic falls within an FDA predefined range relative to the brand name drug. This potential variation in bioequivalence is not thought to be clinically meaningful, however, there are reports of a lack of therapeutic equivalence between some generic medications and the brand name.

Method: Twenty patients at an Anxiety Disorders Clinic who were unknowingly switched to generic citalopram, from Celexa (Lundbeck, Montreal, Quebec, Canada) and experienced a re-emergence of their anxiety symptoms or development of new adverse events are described in this case series report.

Results: The mean time for re-emergence of symptoms or development of adverse events was 3.4 $\pm$ 1.6 weeks (range 0.5 - 8 weeks). All patients re established previous treatment response with a change back to Celexa in a mean time of 3.8 $\pm$ 2.6 weeks (range 0.7 -12 weeks).

Discussion: Given these results, it is important for clinicians to be aware of the potential for loss of treatment effect or symptom re-emergence posed by a switch to a generic agent. Randomized, double blind, controlled investigations would likely provide useful information as current bioequivalence and pharmacological equivalence do not necessarily translate into clinical equivalence.

References:

1. Borgherini G (2003) The Bioequivalence and Therapeutic Efficacy of Generic Versus Brand-Name Psychoactive Drugs. Clinical Therapeutics 25: 1578-1592.
2. Kumet R, Gelenberg AJ (2005) The Effectiveness of Generic Agents in Psychopharmacologic Treatment. Essential Psychopharmacology 104-109.

NR729 Wednesday, May 24, 12:00 PM - 2:00 PM

Primary Care Assessment of the Adult ADHD Self-Report Scale: Preliminary Findings

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the test characteristics of the ASRS, and understand the value and limitations of its use in primary care.

Summary:

Objective: To assess the validity of the Adult ADHD Self-Report Scale (ASRS) in a primary care population.

Methods: Phone screening (ASRS) and structured diagnostic interview (NCS-R Adult ADHD Interview) of 218 patients from a managed care plan serving California and Georgia. Sampling was stratified based on demographics to allow a balanced sample weighted to population estimates. Diagnostic status from the NCS-R interview was assessed relative to the ASRS score, and test characteristics computed.

Results: Diagnostic interviews provided a weighted prevalence estimate of 8.5% adult ADHD in primary care. Using the customary threshold of 4+ items as a positive result, the ASRS showed sensitivity of 39.1% and specificity of 88.3%. Diagnosis rates were similar among those endorsing 3 (29.4%) and 4 (31.9%) of the six items. Allowing for 3 or more items to indicate a positive test, sensitivity increases to 68.5%, and specificity decreases to 76.6%. Actual positive and negative predictive values depend in part on the base rate of the disorder in the sample, which was high in the current study.

Conclusions: The ASRS was more specific than sensitive. A re-evaluation of item cut-points may improve screening performance.Funded by Eli Lilly and Company

References:

1. Kessler RC, Adler L, et al. The World Health Organization adult ADHD self-report scale (ASRS): a short screening scale for use in the general population. Psychol Med 2005; 35(2): 245-256.
2. Adler L, Cohen J, Diagnosis and evaluation of adults with attention-deficit/hyperactivity disorder. Psychiatr Clin North Am 2004; 27(2): 187-201.

NR730 Wednesday, May 24, 12:00 PM - 2:00 PM

Psychotherapy for Depression in Children and Adolescents: Cochrane Systematic Review

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Educational Objectives:

At the conclusion of this presentation, the participants should be familiar with the findings from the best available evidence from RCTs on the efficacy of psychotherapy for depression in children and adolescents.

Summary:

Background:

Depression is a common disorder in children and adolescents. Until recently antidepressants and psychotherapy have both been used to treat this population. However with the possible exception of fluoxetine, there is as yet no convincing evidence that the benefits of antidepressant treatment outweigh the harms, and

recently published NICE guidelines did not recommend antidepressants as first line treatment.

Available reviews of trials of psychotherapy in this age group are outdated, of low quality or not comprehensive, and evidence remains unclear.

Objective:

To synthesize the best available evidence on the efficacy and the harms of psychotherapy for depression in children and adolescents, compared with non-treatment, waiting-list control, attention-placebo or TAU.

Methods:

All randomized controlled trials comparing psychotherapy against the control conditions in the treatment of depression in children and adolescents were included. Comprehensive electronic search has been conducted. Reference search of identified articles and contacting researchers in the field have been done. Two reviewers have independently assessed trial quality and extracted data. A meta-analysis of the data has been performed.

Results:

Initial search identified 495 articles. Of those, 19 RCTs containing 26 comparisons relevant to the present review were included through multiple-stage eligibility check. Nineteen comparisons employed cognitive-behavioral therapy (CBT) as the psychotherapy model of interest.

Psychotherapy was significantly superior to the control conditions immediately after treatment phase, based on response (RR 1.50, 95%CI [1.20, 1.87],p<0.01), but was no longer superior during naturalistic follow-up (1.25, [0.93, 1.68],p=0.14 at 1-6 months and 1.04 [0.86, 1.25],p=0.71 at 6- months after the end of treatment).

Conclusions:

Psychotherapy is superior to the control conditions in children and adolescents at the end of treatment, but the superiority decreases to non-significance during naturalistic follow-up. For psychotherapy models other than Cognitive-Behavior Therapy, there is still little evidence upon which to make any recommendations for clinical practice.

References:

1. Watanabe N, Churchill R, Hunot V, Furukawa TA. Psychotherapy for depression in children and adolescents. (Protocol) In The Cochrane Database of Systematic Reviews 2005, Issue 4.

2. Whittington CJ, Kendall T, Fonagy P, Cottrell D, Cotgrove A, Boddington E: Selective serotonin reuptake inhibitors in childhood depression: systematic review of published versus unpublished data. Lancet 2004; 363(6418): 1341-1345.

NR731 Wednesday, May 24, 12:00 PM - 2:00 PM

Problem Focused Therapy and Placebo or Dextroamphetamine in Treatment of Adults With ADHD

Margaret D. Weiss, M.D. *Children's and Women's Mental Health, 4500 Oak Street, Box 178, Vancouver, BC, V64 3H1, Canada*, Michael B. Wasdell, M.A., Candice Murray, Ph.D., Lily Hechtman, M.D., Brian J. Greenfield, M.D.

Educational Objectives:

Describe the profiles of response of ADHD symptoms to problem focused therapy (PFT) and PFT with stimulant medication in adult patients with ADHD.

Describe the profiles of response of measures of functioningto problem focused therapy (PFT) and PFT with stimulant medication in adult patients with ADHD.

Discuss the temporal differences between the response profiles of PFT and PFT combined with stimulant medication.

Summary:

Background: A manualized psychotherapy for the treatment of adults with ADHD was developed by the authors. Problem Focused Therapy (PFT) provides education about ADHD, support to establish effective coping strategies, and assistance with understanding how to optimize strategies to moderate deficits associated with the disorder.

Objective: To determine whether PFT reduces ADHD symptoms and improves functioning in the absence of active medication, and whether additional benefit is obtained when PFT is combined with stimulant medication.

Method: A subsample (N=48) of patients who were treated in a large multi-site clinical trial and received PFT+placebo or PFT+dextroamphetamine were selected for evaluation. Participants received nine sessions of PFT in conjunction with the scheduled study visits. Medication was titrated by weekly increments over a four week period. Dextroamphetamine was initiated at 5 mg twice daily and was increased to a maximum of 20 mg.

Results: Patients who received PFT+placebo (N=25) showed improvement in ADHD symptoms over the first 20 weeks of the study, p<.001, ES=0.89. Patients receiving PFT+dextroamphetamine also showed significant improvement in ADHD symptoms, p<.001, ES=1.40, at study endopoint but onset of improvement was earlier. The PFT+placebo group showed significant gains in functioning over time, but some of the gains made were lost as the interval between sessions was lengthened. Functional improvement of the PFT+dextroamphetamine group was robust and continued to increase even when sessions were less frequent.**Conclusion:** PFT and stimulant has an earlier onset of action, greater impact, and longer duration of action on functioning than PFT alone.

References:

1. Ratey J, Greenberg MS, Bemporad JR, Lindem KJ. Unrecognized attention-deficit hyperactivity disorder in adults presenting for outpatient psychotherapy. J Child Adolesc Psychopharmacol 1992; 267-75.

2. Safren KA, Otto MW, Sprich S, Winett CL, Wilens TE, Biederman J. Cognitive-behavioral therapy for ADHD in medication-treated adults with continued symptoms. Behav Res Ther 2005; 43:831-842.

NR732 Wednesday, May 24, 12:00 PM - 2:00 PM

Lifetime History of SCID Internalizing Disorders Moderates Stimulant Response in Adults With ADHD

Margaret D. Weiss, M.D. *Children's and Women's Mental Health, 4500 Oak Street, Box 178, Vancouver, BC, V64 3H1, Canada*, Michael Wasdell, M.A., Lily Hechtman, M.D.

Educational Objectives:

Describe the impact of stimulant treatment of adults with with ADHD on ADHD symptoms.

Discuss the differences in stimulant treatment response between patiets who have a lifetime history of internalizing problems versus those who do not.

Understand and discuss the sensitivity of various measures of internalizing symptoms as they relate to adult patients with ADHD

Summary:

Background: A five site study looked at 100 adults with DSM-IV ADHD randomized to treatment with problem focused therapy and either dextroamphetamine, paroxetine, combination or placebo. ADHD responded to dextroamphetamine, and subclinical mood and anxiety symptoms responded to paroxetine, but combined treatment did not yield greater improvements overall. Hamilton Anxiety and Depression scores were below the clinical range

and no treatment yielded significant improvement in internalizing symptoms.

Objective: A post hoc moderator analysis was done to determine if a life time history of any SCID mood or anxiety diagnosis impacted on response to dextroamphetamine.

Results: While Hamilton scores for depression did not moderate response to dextroamphetamine or paroxetine, a life time history of SCID internalizing diagnosis was found to be associated with significantly attenuated response of ADHD symptoms ($p<.05$) and clinician ratings of improvement ($p<.05$) with dextroamphetamine.

Conclusions: Hamilton rating scales are designed for use in patients with clinical depression and are not sensitive to subclinical internalizing symptoms in adults with ADHD. Use of Hamilton scales to control for moderating effects of depression in ADHD outcome are likely to fail to find clinically significant differences in patients with associated depressive and anxiety symptoms versus those without such symptoms. Lifetime SCID internalizing diagnosis may identify sub-populations of ADHD adults who show differential treatment response, even when they are not currently ill.

References:

1. Marks DJ, Newcorn JH, Halperin JM. Comorbidity in adults with attention-deficit/hyperactivity disorder. Ann N Y Acad Sci 2001;931: 216-238.
2. Pliszka SR. Comorbidity of attention-deficit/hyperactivity disorder with psychiatric disorder: an overview. J Clin Psychiatry 1998;59 Suppl 7: 50-58.

NR733 Wednesday, May 24, 12:00 PM - 2:00 PM

Medication Satisfaction Among Adults With ADHD: Long-Term Results From the Quality of Life Effectiveness, Safety, and Tolerability Trial

Margaret D. Weiss *Children's and Women's Mental Health, 4500 Oak Street, Box 178, Vancouver, BC, BC, V64 3H1, Canada*

Educational Objectives:

At the conclusion of this session, participants should be able to

Describe specific aspects of medication satisfaction among adults with attention-deficit/hyperactivity disorder previously treated with an immediate-release stimulant who were switched to therapy with mixed amphetamine salts extended release (MAS XR).

Discuss changes in specific components of satisfaction, including feelings about once-daily dosing, dosing compliance, perceived benefits of stimulant therapy, as well as experience of common adverse effects, such as decreased appetite, seen with MAS XR.

Summary:

Introduction: Long-term medication compliance is low among patients with ADHD. Satisfaction with treatment is key to achieving and sustaining symptom management.

Methods: Medication Satisfaction Survey data were derived from the first 10 weeks of a 30-week, open-label, multisite Quality of Life, Effectiveness, Safety, and Tolerability (QU.E.S.T.) trial in adults (aged >18 years) with ADHD given once-daily mixed amphetamine salts extended release (MAS XR) 10-60 mg/d.

Results: In the intent-to-treat (ITT) population (N=702) 272 adults had previously received stimulant treatment; results from 77 of these subjects who had received an immediate-release stimulant are reported here. At baseline, prior to receiving MAS XR, 48.1% of subjects strongly agreed/agreed that they were satisfied with their immediate-release stimulant, 41.6% were satisfied with how many times per day they needed to take their medication, and 39% rarely missed a dose. After 10 weeks of MAS XR therapy, 72.8% expressed overall satisfaction with MAS XR; satisfaction with once-daily dosing was indicated by 87.0% and 93.5% of subjects, respectively. Reported medication compliance increased; 87.8% rarely missed a dose. Improvements from baseline were also seen in subjects indicating satisfaction with ADHD symptom management after 10 weeks of MAS XR therapy; satisfaction with duration of effect, behavior, attention, and social interactions were indicated by 63.7%, 72.8%, 68.9%, and 52% of subjects, respectively. The rate of decreased appetite was 37.7% and difficulty falling asleep was 14.3%. Improvements in medication satisfaction were maintained or showed further increases at 30 weeks.

Conclusions: Overall medication satisfaction increased among adults with ADHD switched from an immediate-release stimulant regimen to MAS XR 10-60 mg/day. Opportunities for further improvement in satisfaction were apparent with regard to duration of symptom management and social interactions.

This study was funded by Shire Pharmaceuticals Inc.

References:

1. Murphy K, Barkley RA. Attention deficit hyperactivity disorder in adults: comorbidities and adaptive impairments. Compr Psychiatry. 1996;37:393-401.
2. Perwien A, Hall J, Swenson A, et al. Stimulant treatment patterns and compliance in children and adults with newly treated attention-deficit/hyperactivity disorder.

NR734 Wednesday, May 24, 12:00 PM - 2:00 PM

Attention and Deportment Ratings of Transdermal Methylphenidate in ADHD

Sharon B. Wigal, Ph.D. *University of California, Irvine, Child Development Center, 19722 MacArthur Boulevard, Irvine, CA, 92697-4480*, John M. Turnbow, M.D., Howard Abikoff, Ph.D., James J. McGough, M.D., Daniel Sea

Educational Objectives:

At the conclusion of this presentation, the participant should be able to:

Describe the clinical use of the methylphenidate transdermal system (MTS) in pediatric subjects.

Discuss clinician-based SKAMP ratings of attention and behavior of MTS as compared with placebo in a laboratory classroom setting.

Summary:

Objective: Evaluate the efficacy of the methylphenidate transdermal system (MTS) compared with placebo transdermal system (PTS) using the Swanson, Kotkin, Agler, M-Flynn, and Pelham Rating Scale (SKAMP) and subscales in a laboratory classroom setting.

Method: This was a randomized, double-blind, placebo-controlled, laboratory classroom, crossover study, with a 5-week open-label dose optimization phase. Children aged 6-12 years diagnosed with ADHD by DSM-IV-TR criteria were enrolled. Efficacy outcome measures used in the classroom included the SKAMP Rating Scale subscales for attention and deportment evaluated at several time points throughout a 12-hour day.

Results: A total of 79 subjects were evaluated for efficacy. Overall mean SKAMP deportment scores for the MTS treatment group were significantly lower than for the placebo treatment group [3.2 ($\pm$ 0.58) versus 8.0 ($\pm$ 0.58), respectively; $p<0.0001$]. Overall mean SKAMP attention scores also were significantly lower for MTS than for placebo [6.2 ($\pm$0.50) versus 9.9 ($\pm$0.50), respectively; $p<0.0001$]. At all individual post-dose time points measured, treatment with MTS resulted in statistically significantly lower mean SKAMP deportment ($p<0.001$) and attention ($p<0.0001$) change from pre-dose scores compared with placebo.

Conclusion: Treatment with MTS resulted in statistically significant improvements in deportment and attention by SKAMP ratings compared with placebo. MTS was well-tolerated and there were no serious adverse events. MTS may be a safe and effective treatment for pediatric ADHD.

Supported by funding from Shire US Inc.

References:

1. Wigal S, Gupta S, Guinta D, and Swanson J. Reliability and validity of the SKAMP rating scale in a laboratory classroom setting. Psychopharmacology Bull 1998; 34:47-53.

2. Wigal S, McGough JJ, Abikoff H, Turnbow JM, Posner K, and Moon E. Behavioral effects of methylphenidate transdermal system in children with ADHD. Poster presented at the joint meeting of the AACAP and CACAP. Toronto, ON, Canada. October 21, 2005.

NR735 Wednesday, May 24, 12:00 PM - 2:00 PM

Trends in Mental Health Help Seeking Among Minority Dhildren and Adolescents With Serious Behavioral and Emotional Problems in the United States: 2001-2004

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand recent trends in racial disparity in mental health help seeking in children and adolescents in the United States.

Summary:

This study assessed recent trends in racial/ethnic disparities in mental health help seeking in children/adolescents with serious behavioral/emotional problems. Data were drawn from 2 years of the National Health Interview Survey (NHIS) conducted in 2001 and 2004. NHIS is a cross-sectional survey of the US household populations. In children with serious behavioral/emotional problems in 2001 and 2004, mental health help seeking from either mental health professionals or primary care providers were compared across racial/ethnic groups. Serious behavioral/emotional problems were ascertained by the parent version of the Strengths and Difficulties Questionnaire (SDQ), a standardized instrument designed for use in community surveys of children/adolescents. Mental health help seeking for children's problems by parents was ascertained from interviews with parents/guardians. A total of 646 (6.4%) children/adolescents out of 10,367 in 2001 and 566 (6.6%) out of 9,499 in 2004 met criteria for serious behavioral/emotional problems. Logistic regression analysis was used to compare racial/ethnic groups in each year and across years within each racial/ethnic group. Compared to parents of reference group of non-Hispanic white children with serious behavioral/emotional problems, parents of Hispanic children were less likely to seek help from professionals for their child's problems both in 2001 (OR= 0.50, 95% CI=0.31-0.79, $p<0.05$) and in 2004 (OR=0.56, 95%CI= 0.33-0.95, $p<0.05$), as did non-Hispanic black children, but only in the 2001 (OR=0.46, 95% CI=0.28-0.75, $p<0.05$), and not in 2004 (OR=0.88, 95% CI=0.50-1.35, $p=0.65$). Consistent with this finding, in regression analyses within each racial-ethnic group, only the regression model for non-Hispanic black children/adolescents showed a significant coefficient for the survey year variable (OR=2.20, 95% CI=1.14-4.26, $p<0.05$). These findings suggest that initiatives to improve mental healthcare for minorities have resulted in increased mental health help seeking for black children, but not for the other large and growing minority group of Hispanic children.

References:

1. Zimmerman FJ: Social and economic determinants of disparities in professional help-seeking for child mental health problems: evidence from a national sample. Health Serv Res. 2005;40:1514-33.

2. Mojtabai R: Trends in contacts with mental health professionals and cost barriers to mental health care among adults with significant psychological distress in the United States: 1997-2002. Am J Public Health. 2005;95:2009-14.

NR736 Wednesday, May 24, 12:00 PM - 2:00 PM

Employer Burden for Adults Diagnosed with Attention-Deficit/Hyperactivity Disorder Who Received Alternative Therapies

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Educational Objectives:

At the conclusion of this presentation, the participant would know how medical and direct healthcare costs in adults diagnosed with attention-deficit/hyperactivity disorder vary with alternative therapies. A participant would recognize that use of OROS methylphenidate results in reduced medical and direct healthcare costs compared to mixed amphetamine salts extended release or atomoxetine.

Summary:

Objective: To compare 6-month health care costs of adults diagnosed with ADHD receiving extended-release methylphenidate (OROS-MPH, CONCERTA®) to those receiving mixed amphetamine salts extended release (MAS-XR, Adderall XR®) or atomoxetine (Strattera®) from an employer's perspective.

Methods: We examined data from a U.S. employer claims database of 5 million beneficiaries (1999-2004). Analysis was restricted to adults aged 18-64 with at least one diagnosis of ADHD (ICD-9: 314.x) and at least one prescription of OROS-MPH, MAS-XR, or atomoxetine. Adults were required to have continuous eligibility 6 months prior and post their latest therapy initiation and no ADHD therapy in the prior 6 months. Descriptive measures of direct (medical plus pharmaceutical) and medical only costs were computed over 6 months following therapy initiation. Generalized estimating equations (GEE) models were used to compare costs of adults receiving alternative therapies adjusting for demographic characteristics, substance abuse, depression, and the Charlson comorbidity index.

Results: Of the research sample (n=4569), 31.8% received OROS-MPH, 34.0% MAS-XR, and 34.2% atomoxetine. In the 6-month follow-up period, observed direct costs were $2,008 for OROS-MPH, $2,169 for MAS-XR, and $2,540 for atomoxetine-treated adults. The GEE model adjusting for patient characteristics suggested that 6-month medical costs for OROS-MPH-treated adults were $141 less than for the MAS-XR-treated (p=0.0221), and $132 less than for the atomoxetine-treated (p=0.0326). The GEE comparison of direct costs suggested that even after adding drug cost, the costs of OROS-MPH-treated adults were on average $157 less than those of MAS-XR-treated adults (p=0.0167) and $226 less than those of atomoxetine-treated adults (p<0.01).

Conclusion: Over the 6-month period after therapy initiation, adults treated with OROS-MPH on average had lower medical and direct costs than those treated with MAS-XR or atomoxetine, adjusting for patient characteristics.

References:

1. Birnbaum HG, Kessler RC, Lowe SW, Secnik K, Greenberg PE, Leong SA, Swensen AR: Costs of attention deficit-hyperactivity

disorder (ADHD) in the US: excess costs of persons with ADHD and their family members in 2000. Curr Med Res Opin 2005; 21(2):195.

2. Swensen AR, Birnbaum HG, Ben Hamadi R, Greenberg PE, Cremieux PY, Secnik K: Incidence and costs of accidents among attention-deficit/hyperactivity disorder patients. J Adolesc Health 2004; 35(4):346.e1-9.

NR737 Wednesday, May 24, 12:00 PM - 2:00 PM

OROS® MPH Treatment Effects Between Girls and Boys With ADHD

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Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the absence of gender effects on ADHD symptom improvement in girls and boys treated with OROS methylphenidate.

Summary:

Objective: To evaluate symptom improvement in OROS® methylphenidate (MPH)-treated girls and boys with ADHD.

Method: In this analysis, all 850 once-daily OROS MPH-treated children (219 girls and 631 boys 6 to 12 years of age with ADHD) were identified from a prospective, open-label, 3-week, randomized (2:1 OROS MPH or atomoxetine) trial. Initiation and titration of medication was based on each investigator's clinical judgment. Investigators assessed ADHD symptoms and clinical improvement using the ADHD Rating Scale (ADHD-RS), Clinical Global Impression-Severity of Illness (CGI-S) and Clinical Global Impression-Improvement of Illness (CGI-I). Gender differences were measured by ANOVA and Chi-square tests.

Results: Baseline ADHD symptoms were similar between OROS MPH-treated girls and boys (ADHD-RS: 39.1 versus 40.3; CGI-S: 4.52 versus 4.75). At the end of study, ADHD symptom improvement was comparable between girls and boys: change from baseline on ADHD-RS was 20.2 versus 20.5 and CGI-I was 2.26 versus 2.21. Analyses comparing the percentage of subjects achieving response (defined as ≥30%, ≥40%, or ≥50% reduction from baseline ADHD-RS as well as scoring ≤2 on the CGI-I scale) were comparable by gender.

Conclusions: OROS MPH is equally effective in the management of ADHD symptoms in both girls and boys with ADHD.

References:

1. Biederman J, Kwon A, Aleardi M, et at: Absence of gender effects on attention deficit hyperactivity disorder: findings in nonreferred subjects. Am J Psychiatry 2005; 162:1083-1089.

2. Biederman J, Mick E, Faraone SV, et al: Influence of gender on attention deficit hyperactivity disorder in children referred to a psychiatric clinic. Am J Psychiatry 2002; 159:36-42.

NR738 Wednesday, May 24, 12:00 PM - 2:00 PM

OROS® MPH Prescribing Patterns Among Physician Specialties Treating ADHD

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Educational Objectives:

At the conclusion of this session, the participant should be able to understand that community-based pediatricians and psychiatrists are associated with comparable OROS® methylphenidate prescribing patterns in the treatment of attention-deficit/hyperactivity disorder (ADHD).

Summary:

Objective: To examine OROS® methylphenidate (MPH) prescribing patterns among pediatricians and psychiatrists in a community-based setting that treat children with ADHD.

Method: In this analysis, children (6 to 12 years of age) who were treated with OROS MPH and had complete dosage and titration information were identified from a prospective, open-label, 3-week, randomized (2:1 OROS MPH or atomoxetine) trial. Two hundred ninety-seven children were treated by pediatricians (general pediatricians or developmental and behavioral pediatricians) and 343 by psychiatrists (general psychiatrists or child and adolescent psychiatrists). Initiation and titration of medication were based on each investigator's clinical judgment. A titration period was defined as the number of days to the final OROS MPH dosage in the trial. Investigators assessed improvement in ADHD symptoms using the ADHD Rating Scale (ADHD-RS) and Clinical Global Impression - Severity of Illness (CGI-S).

Results: Baseline ADHD symptoms were comparable between children treated by the two specialty groups. Pediatricians and psychiatrists had a similar titration period (7.72 days versus 7.79 days) and prescribed comparable mean final doses of OROS MPH (32.5mg/day versus 33.4mg/day). Distribution of final OROS MPH doses was also similar between pediatricians and psychiatrists (18mg: 22.9% versus 24.1%; 27mg: 23.9% versus 18.7%; 36mg: 38.4% versus 39.1%; 54mg: 13.8% versus 16.9%; 72mg: 1% versus 1.2%; p=NS). At the end of the study, improvement in ADHD symptoms was comparable between the patients treated by either pediatricians or psychiatrists.

Conclusions: In this analysis, community-based physicians including pediatricians and psychiatrists display similar prescribing patterns in treating children with ADHD.

References:

1. Biederman J, Faraone SV: Attention-deficit hyperactivity disorder. Lancet 2005; 366:237-248.

2. Olfson M, Gameroff MJ, Marcus SC, et al: National trends in the treatment of attention deficit hyperactivity disorder. Am J Psychiatry 2003; 160:1071-1077.

NR739 Wednesday, May 24, 3:00 PM - 5:00 PM

Application of Essential Performance Measures for Early Psychosis Treatment

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to evaluate early psychosis services using performance measures developed through a valid process and tested in a service providing care to a population of 1.2 million. In addition the participant will have some standards against which to compare results.

Summary:

Objective: The purpose of this research was to examine the feasibility and utility of applying a previously identified set of consensus derived performance measures to evaluate an early psychosis treatment service.

Methods: This study was conducted in three phases. First the literature was reviewed for performance measures appropriate for early psychosis services. A multi-stakeholder Delphi process was used to identify essential measures. Operational definitions were developed for the measures and attempts were made to collect all measures from a variety of sources including corporate data bases, clinical data bases and chart review. Results were compiled in a report card format. **Results and Conclusions:** 35 measures could be scored including a set of 9 outcome measures. The remaining measures covered 6 the remaining 7 domains of performance recommended for program evaluation. The set of measures provides a core performance framework that assesses the key processes and reflects performance on the program main objectives. These measures can be used to develop standards and when adjusted for baseline population characteristics can serve to benchmark and compare early psychosis treatment services.

References:

1. Hermann RC, Fennerty M, Provost S et al: Process measures for the assessment and improvement of quality of care for schizophrenia. Schizophrenia Bulletin 28:95-104, 2002.
2. Marshall M, Lockwood A, Lewis S, et al: Essential Elements of an early intervention service for psychosis: the opinions of expert clinicians. BioMed Central Psychiatry 4:17, 2004.

NR740 Wednesday, May 24, 3:00 PM - 5:00 PM

The Relationship Between Eszopiclone's Effects on Sleep and Depression in Patients With New Onset MDD and Insomnia

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to evaluate the effect of eszopiclone on depression, as assessed in the HAMD17, that was associated with changes in sleep over 8 weeks of concomitant treatment with fluoxetine.

Summary:

Objective: In a double-blind study, 545 patients who met DSM-IV criteria for new onset MDD and insomnia were randomized to receive either eszopiclone (ESZ) or placebo (PBO) in addition to fluoxetine (FLX). At Weeks 4 and 8, patients receiving FLX+ESZ demonstrated significant improvements in HAMD17 and in subjective sleep parameters relative to those receiving FLX+PBO. This analysis assesses the extent to which the improvements in depression scores may be explained through improvements in sleep.

Methods: Patient-reported sleep parameters were captured weekly, and included sleep latency (SL), wake time after sleep onset (WASO), total sleep time (TST), sleep quality (SQ) and the Insomnia Severity Index (ISI), a validated instrument designed to assess the multiple dimensions of insomnia. HAMD17 was assessed at Weeks 4 and 8. To assess the percent of the treatment effect (PTE) on the HAM-17 attributable to the effect of ESZ on sleep, two statistical models were used. Model 1 had treatment as the only explanatory variable for NDF improvements (estimated treatment effect $beta_1$). In Model 2, both treatment and the post-dose sleep parameters were explanatory variables (estimated effect $beta_2$). Estimates from both models were used in the following equation: $PTE=100(beta_1 - beta_2)/beta_1$. (PTEs > 100% were set to 100%).

Results: At Week 4, PTEs were ISI (69%), SQ (54%), WASO (49%), SL (28%), and TST (19%). At Week 8, PTEs decreased for all parameters: ISI (44%), SQ (5%), WASO (15%), SL (0%), and TST (0%).

Conclusion: In this analysis, more of the treatment effect on depression at Week 4 was explainable through changes in sleep than at Week 8, and the sleep parameters having the greatest effects were the ISI, SQ, and WASO.

Support for this study provided by Sepracor Inc.

References:

1. Krystal AD, Walsh JK, Laska E, Caron J, Amato DA, Wessel TC, Roth T: Sustained efficacy of eszopiclone over 6 months of nightly treatment: results of a randomized, double-blind, placebo-controlled study in adults with chronic insomnia. Sleep 2003;.
2. Zammit GK, McNabb LJ, Caron J, Amato DA, Roth T: Efficacy and safety of eszopiclone across 6-weeks of treatment for primary insomnia. Current Medical Research and Opinion 2004; 20(12):1979-1991.

NR741 Wednesday, May 24, 3:00 PM - 5:00 PM

Binge Drinking and Alcohol-Related Problems in a Catchment Area Study in Brazil

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to:

1. Get information about binge drinking, a harmful pattern of alcohol consumption related to acute health problems and social consequences.
2. Recognize the magnitude of binge drinking in the São Paulo Epidemiologic Catchment Area Study in Brazil.
3. Verify gender differences in the presentation of problems related to this pattern of alcohol consumption.
4. Be able to compare the findings with data from other countries.

Summary:

Objectives Quantify episodes of binge drinking among adults in a defined Catchment Area in São Paulo, to characterize adults who engage in binge drinking, gender differences, alcohol-related problems and sociodemographic outcomes.

Methods Data were derived from São Paulo Catchment Area study and were based on a representative sample (N= 1,464) of the adult population living in two defined boroughs of the city of São Paulo. The pattern of binge-drinking and its adverse outcomes were investigated in their relationship with sociodemographic features. The assessment of psychopathology was made by CIDI 1.1, yielding ICD-10 diagnoses.

Results Binge drinking defined as consumption of 5 or more drinks on at least 1 drinking day for men and 4 or more drinks for women was significantly related with gender (male), age (younger groups) marital status (divorced and single), employment (unemployed), alcohol intake (heavy drinking) and problems (personal, work, driving and health problems). Overall, lifetime prevalence of binge drinking was 16.3%, three times more prevalent among males than females (almost 25.41% compared to 9.83%). Men referred more problems than women (63% versus 50%), most of the problems are related to violence (14.5%), while women referred more psychological problems (10.3%).

Conclusion Binge Drinking is common among most strata of São Paulo adults, including among those aged 18 or older. Binge drinking is strongly associated with alcohol impaired driving, violence, psychological, personal and health problems. Effective interventions to prevent morbidity associated with binge drinking

should be widely adopted, including screening patients for alcohol abuse in accordance with national guidelines.

References:

1. Andrade L, Walters EE, Gentil V, Laurenti R . Prevalence of ICD-10 mental disorders in a catchment area in the city of São Paulo, Brazil. Soc Psychiatry Psych Epidemiol 2002; 37:316 - 327.
2. Leifman, H., Hemstrom, O. & Ramstedt, M. (2001) The ECAS-survey on drinking patterns and alcohol related problems. In: Norstrom, T., ed. Alcohol in Post War Europe,pp. 105'126. Stockholm: National Institute of Public.

NR742 Wednesday, May 24, 3:00 PM - 5:00 PM

Severity of Personality Disorders and Suicide Attempts

Enrique Baca-García *Jimenez Diaz Foundation, Department of Psychiatry. avda. Reyes católicos, 2, Madrid, 28040, Spain*, Hilario Blasco-Fontecilla, M.D., Luis Jimenez-Trevino, Dolores Braquehais, Jose de Leon, Jeronimo Saiz-Ruiz

Educational Objectives:

At the conclusion of this presentation, the participant should be able to know that suicide attempts in subjects diagnosed with a diffuse personality disorder are not more severe than those on subjects with simple personality disorders or with no personality disorders at all.

Summary:

Objective: individuals diagnosed with a *diffuse personality disorder* (DPD) may have greater psychopathology. Our main hypothesis was that individuals diagnosed with a DPD would be more prone to have more lethal suicide attempts and to have a history of multiple suicide attempts than those with a simple PD.

Method: a sample of 446 suicide attempters seen at the emergency room of two general hospitals in Madrid (Spain) were assessed. The *International Personality Disorders Examination (IPDE)* screening questionnaire was used to diagnose personality disorders. An adjusted cut-off point was used in order to increase specifity and lower the rate of false positives. Different measures - *Lethality Rating Scale (LRS), Weisman & Worden Scale, Beck Suicide Intent Scale* (SIS) and, finally, the *Barratt Impulsivity Scale* (BIS) - were used to assess lethality and impulsivity. Suicide attempters (SA) with no PD, SA with a simple PD and, SA with a diffuse PD were compared.

Results: contrary to our expectation, subjects diagnosed with a *diffuse PD* have no more severe suicide attempts. However, they are more likely to have a history of prior suicide attempts (X^2= 25.085; df= 4; p< 0.001). After controlling for age and gender, differences were only significant in the youngest group age (18-35 years) (X^2= 18.026; df= 4; p = 0.001) and in women (X^2= 25.810; df= 4; p < 0.001).

Conclusions: individuals diagnosed with a diffuse personality disorder are more likely to have a history of suicide attempts.

References:

1. Tyrer P, Johnson T. Establishing the severity of personality disorder. Am J Psychiatry 1996;153(12),1593-97.
2. Pallis DJ & Birtchnell J. Serious of suicide attempt in relation to personality. Br J Psychiatry 1977;130:253-259.

NR743 Wednesday, May 24, 3:00 PM - 5:00 PM

Ropinirole Improves Restless Legs Syndrome Symptoms in RLS Patients With Disturbed Sleep

Philip M. Becker, M.D. *Sleep Medicine Associates of Texas, 8140 Walnut Lane, Suite 100, Dallas, TX, 75231*, Carolyn B. Watson, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to assess the effects of ropinirole, a dopamine agonist, in patients with moderate-to-severe primary Restless Legs Syndrome (RLS) who are experiencing disturbed sleep.

Summary:

Introduction: RLS is a chronic neurological disorder, characterized by an irresistible urge to move the legs. Disturbed sleep is a common presenting symptom, and insomnia medications are sometimes prescribed; however, these are not likely to treat the underlying disorder.

Methods: In three 12-week, double-blind, flexible-dose studies - TREAT RLS 1, 2, and US (protocols 101468/190, 194, and 249, respectively) - patients with moderate-to-severe primary RLS were randomized (n=934) to once-daily placebo or ropinirole, 0.25-4.0 mg/day titrated as needed and tolerated, 1-3 hours before bedtime. *Post-hoc* analysis of pooled data assessed treatment efficacy in patients who responded on Questions 3 (sleep not quiet; n=453), 7 (trouble falling asleep; n=411), or 8 (wake and trouble falling asleep again; n=367) of the Medical Outcome Study (MOS) Sleep Scale at baseline, indicating at least moderately disturbed sleep.

Results: At Week 12 last observation carried forward, change from baseline in International Restless Legs Scale total score showed a statistically significant treatment difference in favor of ropinirole among patients with impaired sleep responses at baseline to MOS Questions 3 (adjusted mean treatment difference [AMTD]: -2.9; 95%CI: -4.6, -1.2; p<0.001), 7 (AMTD: -3.4; 95%CI: -5.2, -1.6; p<0.001), and 8 (AMTD: -4.6; 95%CI: -6.5, -2.7; p<0.001). Also, a statistically significantly greater proportion of ropinirole patients, compared with placebo, were rated as responders (much or very much improved) on the Clinical Global Impression-Improvement scale among patients with impaired sleep responses on MOS Questions 3, 7, and 8 (odds ratios = 1.8 [95%CI: 1.2, 2.6; p=0.003], 2.2 [95%CI: 1.4, 3.2; p<0.001], and 2.2 [95%CI: 1.4, 3.4; p<0.001], respectively).

Conclusions: Ropinirole improves RLS symptoms in patients with moderate-to-severe primary RLS experiencing disturbed sleep; in addition, a greater proportion of ropinirole-treated RLS patients with disturbed sleep were classified as responders to treatment.

Supported by: GlaxoSmithKline Research & Development.

References:

1. Hening W et al. Sleep Med 2004; 5: 237'46.
2. Saletu B et al. Neuropsychobiology 2000; 41: 181'9.

NR744 Wednesday, May 24, 3:00 PM - 5:00 PM

Impulsivity and Alcoholism: Reduced Frontal Activity

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Educational Objectives:

At the conclusion of this presentation, the participants should be able to recognize the high prevalence of high impulsivity among alcoholism and other externalizing disorders. This presentation will also demonstrate neurobiological and genetic views to dissect the complex phenotypes in the disinhibitory disorders.

Summary:

BACKGROUND: Impulsivity is an important manifestation of many psychiatric disorders, including substance-related disorders. These disinhibitory disorders have a similar underlying genetic diathesis, with each disorder representing a different expres-

sion of the same underlying genetic liability. There is evidence for the P3 amplitude of the event-related potential (ERP) as a phenotypic marker for the risk of alcoholism. The aims of this study were to assess the potential role of impulsivity underlying the pathogenesis of alcohol dependence, and its correlations with P3 amplitude.

Methods: Subjects included healthy adult controls (n=58) and adults who met DSM-IV criteria for alcohol dependence but no other Axis I diagnoses (n=57).Cognitive neural activities were assessed with a visual Extended Release P oddball task in which rare target P3s were recorded from 61 scalp electrodes. Impulsivity was measured using a self-report questionnaire (Barratt Impulsivity Scale, BIS, version 11). Source localization of surface amplitude values were plotted and analyzed using a low-resolution brain electromagnetic tomography (LORETA).

Results: Alcoholics manifested reductions in P3 amplitudes ($p<0.0001$). Significantly reduced activation in the cingulate, medial and superior frontal regions in LORETA was seen in alcoholics, as well as high impulsive subjects. Alcoholics had significantly higher scores on the BIS ($p<0.0001$). There were significant negative correlations between total scores in BIS and P3 amplitude ($p=0.003$, Pz; $p=0.007$, Cz).

Conclusions: Our results demonstrate a strong frontal focus of reduced activation in alcoholics and individuals with higher impulsivity during processing of visual targets. The findings suggest that impulsivity may be an important factor that underlies the pathogenesis of alcohol dependence. Studies are underway to examine the relationship between impulsivity and Extended Release P characteristics in offspring of alcoholics, to determine whether this relationship antecedes the development of alcoholism and to identify genes associated with the underlying predisposition involved in disinhibitory disorders.

References:

1. Begleiter H, Porjesz B, Bihari B, Kissin B. Event-related brain potentials in boys at risk for alcoholism. Science. 1984; 225:1493-6.

2. Porjesz B, Rangaswamy M, Kamarajan C, Jones KA, Padmanabhapillai A, Begleiter H. The utility of neurophysiological markers in the study of alcoholism. Clinical Neurophysiology. 2005; 116:993-1018.

NR745 Wednesday, May 24, 3:00 PM - 5:00 PM

Identification of High Utilizer Patients of Primary Care Resources With Major Depression

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Educational Objectives:

At the conclusion of this presentation, the participant should understand that high utilizer patients in primary care who were identified with previously undiagnosed and untreated major depression, were of employable age and underprivileged. The participant should know that systematic screening may facilitate adequate diagnosis and treatment of the underlying disorder.

Summary:

Objective: Approximately 25% of so-called high utilizer patients of medical care resources are estimated to suffer from depression. A large proportion of these individuals remain undiagnosed and untreated. This study aims to show the effectiveness of a systematic screening and treatment program in primary care with regard to depression severity, quality of life, and medical resource utilization.

Method: High utilizer patients in primary care were identified using the Brief Psychiatric Health Questionnaire. Those who screened positive with depressive symptoms were diagnosed using the DIA-X, a standardized diagnostic interview, performed by trained and supervised interviewers. Patients with major depression were included in a randomized, prospective intervention study comparing a.) a 6-month treatment program of pharmacotherapy, standardized information, and physician and patient counseling or b.) 6 months of usual medical care. Both interventions were followed by a 6-month observation period.

Results: Out of approximately 19,000 patients in 31 primary care practices, 1,649 high utilizer patients could be identified. Of these individuals, a total of 227 were screened as having depressive symptoms. Of the patients verified by DIA-X, 35% had other psychiatric diagnoses, 16% had severe suicidal thoughts and were assigned to specialized treatment, and 70% were not eligible for various reasons. The baseline characteristics of the patients included in the trial were: 29% male, 71% female, mean age 47.8 (SD 12.8), 46% living alone, 23% unemployed, and 59% on sick leave.

Conclusion: In our study, high utilizer patients in primary care who were identified with previously undiagnosed and untreated major depression were of employable age and underprivileged. Systematic screening may facilitate adequate diagnosis and treatment of the underlying disorder.

References:

1. Katzelnick DJ, Simon GE, Pearson SD, Manning WG, Helstad CP, Henk HJ, Cole SM, Lin EH, Taylor LH, Kobak KA: Randomized trial of a depression management program in high utilizers of medical care. Arch Fam Med 2000;9:345-351.

2. Schoenbaum M, Unützer J, Sherbourne CD, Duan N, Rubenstein LV, Miranda J, Meredith L, Carney M, Wells KB: The cost-effectiveness of practice-initiated quality improvement for depression: results of a randomized, controlled trial. JAMA 2001; 284: 132.

NR746 Wednesday, May 24, 3:00 PM - 5:00 PM

Peritraumatic and Acute Stress Predicting Persistent Posttraumatic Stress in a Group of Industrial Disaster Survivors

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize peritraumatic dissociation and distress and acute stress symptoms predicting ptsd

Summary:

Objective: Our longitudinal study aimed at assessing the power of early psychological predictors in prospectively predicting persistent Posttraumatic Stress Disorder (PTSD) symptoms.

Methods: One hundred and twenty-nine injured victims of the explosion of a petrochemical plant filled-out self-report questionnaires on their symptoms of acute stress disorder (ASD) and of depression (Wave I: 5-10 weeks posttrauma), and peritraumatic responses of distress and dissociation (Wave II: 6 months posttrauma). These early predictors were regressed in a subsample of (n=50) participants comprised of the 19 individuals diagnosed with current PTSD 18 months posttrauma (Wave IV) and the 31 individuals without PTSD with the lowest symptom score.

Results: All four early psychological predictors were significantly correlated with PTSD at 18 months posttrauma. In separate multi-

variate logistic regression models, the best predictors of persistent PTSD symptoms were peritraumatic distress and ASD symptoms.

Conclusions: This replicates our previous finding that peritraumatic distress and dissociation and ASD are robust predictors of PTSD. Such symptoms may be of use at the emergency room and elsewhere, for identifying at an early stage disaster survivors at highest risk of persistent PTSD symptoms.

References:

1. Birmes P, Brunet A, Carreras D, Ducasse JL, Charlet JP, Lauque D, Sztulman H, Schmitt L. The predictive power of peritraumatic dissociation and acute stress symptoms for posttraumatic stress symptoms: a three-month prospective study. Am J Psychiatry.
2. Birmes PJ, Brunet A, Coppin-Calmes D, Arbus C, Coppin D, Charlet JP, Vinnemann N, Juchet H, Lauque D, Schmitt L: Symptoms of peritraumatic and acute traumatic stress among victims of an industrial disaster. Psychiatr Serv 2005; 56:93-95.

NR747 Wednesday, May 24, 3:00 PM - 5:00 PM

Post-Traumatic Stress in Children 18-24 Months After an Industrial Disaster

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to screen out children and families experiencing the most severe problems in the aftermath of disasters

Summary:

Objective: To evaluate family functioning, symptoms of Posttraumatic Stress Disorder (PTSD) and depression in parents, and examined how these factors relate to PTSD symptoms in children 18-24 months after the explosion of a petrochemical plant.

Methods: We used the Child Post Traumatic Stress Reaction Index, the Children's Depression Inventory, and the Mini International Neuropsychiatric Interview (MINI-Kid). For parents, the PTSD Check-List Scale, the Beck Depression Inventory and the MINI were used. Parents and children completed the Family Adaptability and Cohesion Evaluation Scale. Bivariate analyses were completed by a logistic regression including variables linked to the children's PTSD status.

Results: Among the 106 children evaluated 12 had full PTSD and 37 had partial PTSD, showing 49 children with PTSD+ status. Having a family member was by the child's side at the time of the explosion, a PTSD+ status in the mother, being female, and witnessing injuries were all factors significantly associated with a PTSD+ status. Fusional or rigid family functioning was significantly associated with PTSD- status.

Conclusion: In the aftermath of disasters family assessment should take into account the following: the experience of the trauma for each family member; the fact that whether or not family members were exposed; and feelings of family closeness or remoteness. This type of assessment protocol could be useful in the identification of families experiencing the most severe problems in the aftermath of disasters.

References:

1. Birmes P, Brunet A, Coppin-Calmes, D Arbus C, Coppin D, Charlet JP, Vinnemann N, Juchet H, Lauque D, Schmitt L. Peritraumatic and Acute Traumatic Stress Symptoms among Victims of an Industrial Disaster. Psychiatr Serv 2005; 56: 93-95.
2. Laor N, Wolmer L, Cohen DJ. Mothers' functioning and children's symptoms 5 years after a SCUD missile attack. Am J Psychiatry 2001; 158: 1020-1026.

NR748 Wednesday, May 24, 3:00 PM - 5:00 PM

Association of Sleep Complaints and Medical Conditions: Prevalence, Use of Services, and Risk Factors in an Elderly Community Survey

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Educational Objectives:

Estimated prevalence of sleep problems in the elderly community population is high. In this investigation we wanted to investigate the association of sleep complaints with physical diseases, self rated health, psychiatric morbidity and the use of services. At the conclusion of this presentation the participant shoud be able do recognize possible risk factors of insomnia within elderly subjects

Summary:

Objective: The main purpose of this study is to investigate the association of sleep complaints with physical and psychiatric morbidity in people aged 60 years and over. Method: Population-based random sample of 7040 household residents, aged 60 years and over, examined in a face to face interview.

Results: The overall prevalence of insomnia is 33.7% (95% CI: 32.5 - 34.8%); higher in women 37.2% (95% CI: 35.8 - 38.6%), than in men 27.4% (95% CI: 25.4 - 29.3%) ($p < 0.0001$). A substantial burden of physical/mental morbidity is associated with the presence of sleep complaints,51% (95% CI: 49 - 53%), mainly psychiatric morbidity, hypertension, urinary infection and varicose veins. The rate of medical consultations, 78% (95% CI: 76.0 - 79.9%) and hospitalizations (33 to 65%) increases in the presence of sleep complaints. In logistic regression models, almost all health problems investigated emerged as independent predictors of insomnia as well as impaired quality of life. Age has a negative effect on sleep complaints. The odds of psychiatric morbidity are also affected by income, ethnicity, origin (urban/rural), and gender.

Conclusion: The association of sleep complaints and physical/psychiatric morbidity in late life is statistically strong in this surveyed population.

References:

1. Foley D, Ancoli-Israel S, Britz P, Walsh J. Sleep disturbances and chronic disease in older adults: results of the 2003 National Sleep Foundation Sleep in America Survey. J. Psychosom. Res.2004; 56:497-502.
2. Ohayon MM . Relationship between chronic painful physical condition and insomnia. J. Psychitr. Res. 2005; 39:151-9.

NR749 Wednesday, May 24, 3:00 PM - 5:00 PM

The Optimal Cut-Off Value of Elevated Homocysteine in Predicting Alcohol Withdrawal Seizures

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Educational Objectives:

At the end of this presentation, the participants should be able to recognize patients admitted for alcohol intoxication at risk for withdrawal seizures.

Summary:

Introduction: Higher homocysteine levels were found in actively drinking patients with alcohol dependence. Recent studies have shown that high homocysteine levels are associated with alcohol withdrawal seizures. The aim of the present study was to calculate the best predictive cut-off value of plasma homocysteine levels in actively drinking alcoholics (n=88) suffering from first-onset alcohol withdrawal seizures.

Methods: The present study included 88 alcohol dependent patients whereby 18 patients suffered from a first-onset withdrawal seizures. All patients were active drinkers and had an established diagnosis of alcohol dependence according to the Diagnostic Statistical Manual for Mental Disorders (DSM-IV). Sensitivity and specificity were calculated using every homocysteine plasma level found in the study population as cut-off value. Bayes-theorem was used to calculate positive (PPV) and negative (NPV) predictive values for all cut-off values used.

Results: Positive predictive values ranged from 0.23 to 0.745 whereby the maximum was reached at a homocysteine plasma level of 41.7 μmol/l. However, the highest combined sensitivity and specificity was reached at a homocysteine plasma cut-off value of 23.9 μmol/l.

Discussion: Homocysteine levels above this cut-off value on admission are a useful screening tool to identify actively drinking patients at higher risk of alcohol withdrawal seizures. Therefore patients who do not belong to this high risk group or are below of this critical predictive cut-off value might avoid the potentially side effects of antiepileptic medication (i.e. carbamazepine) administered in alcohol withdrawal

References:

1. Bayerlein K, Hillemacher T, Reulbach U, Mugele B, Sperling W, Kornhuber J, Bleich S: Alcoholism-associated hyperhomocysteinemia and previous withdrawal seizures. Biol Psychiatry, 2005, 57:1590-1593.
2. Bleich S, Degner D, Bandelow B, Von Ahsen N, Ruther E, Kornhuber J: Plasma homocysteine is a predictor of alcohol withdrawal seizures. Neuroreport, 2000, 11:2749-2752.

NR750 Wednesday, May 24, 3:00 PM - 5:00 PM

Comparison Between 12-Session and One-Year Dynamic Psychotherapies in the Treatment of Adjustment Disorder

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Educational Objectives:

This study focuses on the relative benefits of different length of dynamic therapy. The educational benefit is in learning about the limitations and advantages of short-term psychotherapy compared to long-term psychotherapy.

Summary:

The optimal length for psychotherapeutic intervention in the treatment of adjustment disorders is unknown. This knowledge is pertinent in this day and age when administrative considerations often contaminate clinical decisions. Outpatients diagnosed with Adjustment Disorder by SCID (n=66) were randomly assigned to either a 12-session ("short") or 1-year ("long") dynamic psychotherapy. Self-assessment by patients included the Symptom Checklist-90 (SCL-90) for symptom profile, Mental Health Inventory (MHI) for welfare, distress and satisfaction, the Barron questionnaire for ego strength, and a therapeutic alliance questionnaire. Treatment outcome assessed by psychotherapists included the Clinical Global Severity (CGS), Improvement (CGI) and Global Assessment of Functioning (GAF). Forty-five patients (26 long, 19 short) completed treatment. No between-group differences were observed at baseline. At the end of 12 sessions, while no objective improvement was observed (by psychotherapists), in both the whole group, and each of the 2 groups, patients' subjective symptom level and distress measures (SCL-90, MHI) significantly improved. At the end of 12 sessions, the "long" protocol group showed significantly greater objective (CGS, GAF), but not subjective improvement compared to the "short" protocol group. In the "long" group, significant improvement was observed at the end of treatment (1 year) compared to both the 12-session point and baseline in all parameters. Comparing end points of both groups, psychotherapists assessed the "long" protocol patients' clinical (CGI) and functional (GAF) outcome as significantly better than the "short" protocol patients', while subjective assessment improved significantly in the Global Severity Index (SCL-90) only. MHI and therapeutic alliance results did not differ. In conclusion, dynamic psychotherapy for adjustment disorder produces significant symptomatic and functional relief already after 12 sessions. However, patients undergoing 1-year dynamic psychotherapy show a greater improvement already after 12 sessions and are significantly less symptomatic at the end of treatment compared to patients who had only 12 sessions.

References:

1. Straker M: Brief psychotherapy in an outpatient clinic: Evolution and evaluation. American Journal of Psychiatry 1968; 124: 1219-1225.
2. Robinson LA, Berman JS, Neimeyer RA: Psychotherapy for the treatment of depression: A comprehensive review of controlled outcome research. Psychological Bulletin 1990; 100: 30-49.

NR751 Wednesday, May 24, 3:00 PM - 5:00 PM

Ropinirole Extended Treatment Coverage in Restless Legs Syndrome: Patient- and Physician-Reported Efficacy

Richard K. Bogan, M.D. *SleepMed of South Carolina, Department of Medicine, SleepMed, 1333 Taylor Street, Columbia, SC, 29201*, David A. Hosford, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to identify that some patients with Restless Legs Syndrome may require extended treatment coverage and that, based on both physician- and patient-rated scales, ropinirole (a dopamine agonist) provides rapid and effective relief of symptoms in such patients.

Summary:

Introduction: Ropinirole is an FDA-approved medication for moderate-to-severe primary RLS.[1,2] Patients with RLS experiencing symptom onset in the late afternoon or early evening may benefit from extended treatment coverage. This double-blind, flexible-dose study (protocol: 101468/100013) examined the efficacy, including speed of onset, of ropinirole given in divided doses in this population.

Methods: Patients (n=363) with primary RLS and a baseline International Restless Legs Scale (IRLS) total score ≥20 received ropinirole or matched placebo, 0.5-6.0mg/day, in two divided doses (1 hour before usual symptom onset and 3-8 hours later). The primary endpoint was the change from baseline to Week 12 last observation carried forward (LOCF) in the IRLS total score. Secondary endpoints included the proportions of responders (much/very much improved) on patient-rated Patient Global Improvement (PGI) and physician-rated Clinical Global Impression-Improvement (CGI-I) scales.

Results: The improvement in IRLS total score was significantly greater with ropinirole compared with placebo at Week 12 LOCF (adjusted mean treatment difference [AMTD]: -4.1; 95% CI: -6.1, -2.1; p<0.001) and at all other visits including Day 3 observed case (OC) (AMTD: -2.8; 95% CI: -4.5, -1.2; p<0.001). The proportions of PGI and CGI-I scale responders were also significantly greater for the ropinirole group compared with the placebo group at all assessment points; for example, PGI scale: Day 1 OC odds ratio (OR): 2.0; 95% CI: 1.2, 3.4; p=0.013, and Week 12 LOCF OR: 3.4; 95% CI: 2.1, 5.4; p<0.001; CGI-I scale: Day 3 OC OR: 2.6; 95% CI: 1.5, 4.4; p<0.001, and Week 12 LOCF OR: 2.4; 95% CI: 1.6, 3.8; p<0.001. The safety profile was similar to that in once-daily-dosing studies (e.g. TREAT RLS US).

Conclusions: Based on both patient- and physician-rated scales, ropinirole provides rapid and sustained symptom relief in RLS patients needing extended treatment coverage.

Supported by: GlaxoSmithKline Research & Development.

References:

1. Trenkwalder et al. J Neurol Neurosurg Psychiatry 2004; 75: 92'7.

2. Walters et al. Mov Disord 2004; 19: 1414'23.

NR752 Wednesday, May 24, 3:00 PM - 5:00 PM

Ropinirole: Effective for Restless Legs Syndrome Regardless of Age at Onset

Richard K. Bogan, M.D. *SleepMed of South Carolina, Department of Medicine, SleepMed, 1333 Taylor Street, Columbia, SC, 29201*, Richard P. Allen, Ph.D., Nancy L. Earl, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to identify that the response to ropinirole treatment in patients with Restless Legs Syndrome (RLS) appears to be unaffected by age at RLS symptom onset.

Summary:

Introduction: Restless Legs Syndrome (RLS) is a chronic neurological disorder characterized by an irresistible urge to move the legs.[1] Two phenotypes have been proposed, based on age at initial RLS symptom onset: 'early' (before age 45) and 'late'.[2] These phenotypes may be due to differing pathophysiology, which may have implications for treatment response.

Methods: Pooled data from three 12-week, multicenter, double-blind, flexible-dose, placebo-controlled trials of ropinirole in patients with moderate-to-severe primary RLS (TREAT RLS 1, 2, and US; protocols 101468/190, 194, and 249, respectively) were analyzed *post-hoc* to explore treatment response according to age at symptom onset, fitting linear and logistic regression models. In each study, patients were randomized to ropinirole, 0.25-4.0 mg/day titrated as needed and tolerated, or placebo, once daily, 1-3 hours before bedtime. Treatment response was assessed according to change in International Restless Legs Scale (IRLS) total score and the proportion of patients classed as responders (much or very much improved) on the Clinical Global Impression - Improvement (CGI-I) scale.

Results: Age at RLS symptom onset was similarly distributed in the ropinirole and placebo groups. Statistical modeling, using age at onset as a continuous variable, found no statistically significant interaction between age at onset and treatment arm, based on change in IRLS total score (p=0.7577) or response on the CGI-I scale (p=0.3559). Following ropinirole treatment, mean changes from baseline in IRLS total score were similar for early- and late-onset patients (-11.9 in both groups at Week 12 last observation carried forward), as were final ropinirole doses (mean 2.0 and 2.1 mg in early- and late-onset groups, respectively).

Conclusions: These data suggest that ropinirole provides effective relief of symptoms regardless of age at RLS symptom onset.

Supported By Funding From: GlaxoSmithKline Research & Development.

References:

1. Allen RP, Picchietti D, Hening WA et al. Sleep Med 2003; 4: 101'119.

2. Allen RP, Earley CJ. Sleep Med 2000; 1: 11'19.

NR753 Wednesday, May 24, 3:00 PM - 5:00 PM

Day-of-the-Week Drinking Variability in Alcohol-Dependent Patients and Efficacy of Pharmacotherapy With Long-Acting Naltrexone

Michael J. Bohn *Aurora Behavioral Health, 1220 Dewey Ave, Wauwatosa, WI, 53213*, David R. Gastfriend, Ari Illeperuma, Bernard Silverman

Educational Objectives:

At the conclusion of this session, participants should better understand the intraweek variations in drinking behavior among alcohol-dependent patients and their response to treatment with long-acting naltrexone (LA-NTX).

Summary:

Background: Recently, a large placebo-controlled, randomized trial showed efficacy of LA-NTX over a 24-week period in the treatment of alcohol dependence. Potential variations in day-to-day drinking across the week, particularly in relation to pharmacotherapy, have not been closely studied.

Objective: To perform a post-hoc analysis of intraweek differences in drinking behavior among alcohol-dependent patients who participated in a phase III clinical study of LA-NTX versus placebo.

Method/Design: In a 6-month, randomized, multi-site (24 centers), double-blind, placebo-controlled study, 624 alcohol-dependent adults were randomized to receive: LA-NTX 380 mg (n = 205), or 190 mg (n = 210) or placebo (PBO, n = 209) monthly in combination with 12 sessions of low-intensity psychosocial therapy. Drinking patterns before and after treatment were compared for weekdays (Sundays to Thursdays) versus weekends (Friday, Saturday)

Results: All treatment groups showed little variation in the pattern of drinking on weekdays and increased drinking on weekends. Prior to study entry, the median percentage of patients with heavy drinking on weekends was 78% versus 62% for weekdays (p<0.0001). On weekends, these percentages were reduced to 17% for LA-NTX 380 mg and 28% for PBO (p=0.011); on weekdays, these percentages were 8% for LA-NTX 380 mg and 15% for PBO (p=0.003). A similar pattern of reduction was seen with the number of drinks consumed per day.

Conclusion: Heavy drinking was more common on Fridays and Saturdays compared to the rest of the week. Treatment with LA-NTX 380 mg, in combination with counseling, significantly reduced heavy drinking on both weekdays and weekends in comparison with placebo.

References:

1. Grant BF, Dawson DA, Stinson FS, Chou SP, Dufour MC, Pickering RP. The 12-month prevalence and trends in DSM-IV alcohol abuse and dependence: United States, 1991-1992 and 2001-2002, Drug Alcohol Depend 2004;74;223-34.

2. Garbutt JC, Kranzler HR, O'Malley SS, et al. Vivitrex Study Group. Efficacy and tolerability of long-acting injectable naltrex-

one for alcohol dependence: a randomized controlled trial. JAMA 2005;293;1617-25.

NR754 Wednesday, May 24, 3:00 PM - 5:00 PM

Mood and Cognitive Variability in Women With Alcohol Abuse Problems

Rudy C. Bowen, M.D. *University of Saskatchewan, Department of Psychiatry, Ellis Hall Room 123, 103 Hospital Drive, Saskatoon, SK, S7N 0W8, Canada*

Educational Objectives:

At the conclusion of this presentation the participant should be able to recognize the contribution for variable mood and attention to distress and disability.

Summary:

Objective:

To determine whether women with alcohol abuse problems (n= 22) show:

1. Higher mood variability (MV) than student controls (n=22),
2. Whether mood variability is associated with attention variability.

Method: 22 women with alcohol abuse during the 3rd week of residential addiction treatment completed the MINI Interview and Conners' CPT. All subjects completed a diary with 4 Visual Analogue Scales (VAS) for depressed, anxious, angry, high moods twice a day for 7 days. They also completed rating scales for depression, anxiety, hypomania and the TEMPS-A questionnaire. Attention variability was determined from response-speed-variability of the CPT, and mood variability from the VAS mean square successive difference.

Results: Subjects showed high diagnostic comorbidity and scored higher on the mood rating scales. Subjects did not differ from controls on the Mean VAS scales, but they showed more mood variability on depressed, anxious and angry scales. Depressed, anxious or high mood variability was correlated with Sustain Attention response-speed-variability and Sustain Attention response-speed-consistency.

Conclusion: Women with alcohol abuse problems show higher variability of negative moods than controls. The correlation between mood and attention variability suggests an innate difficulty with regulation.

References:

1. Bowen RC, Clark M, Baetz M: Mood swings in patients with anxiety disorders compared with normal controls. J Affect Disord 2004; 78: 185-192.
2. Clark L, Iversen SD, Goodwin GM: Sustained attention deficit in bipolar disorder. Br J Psychiatry 2002; 180: 313-319.

NR755 Wednesday, May 24, 3:00 PM - 5:00 PM

Patients With Anger Control Problems Show High Mood and Anger Variability

Rudy C. Bowen *University of Saskatchewan, 103 Hospital Drive, Saskatoon, SK, S7N 0W8, Canada*, Adelugba Olajide, Presse Cindy, Ph.D., Mela Mansfield

Educational Objectives:

1. To recognise the concept of variability of mood and anger in forensic patients
2. To understand the relationship between anger expression and facets of personality, temparament and other emotions in forensic patients.

Summary:

Objective

1. To study whether forensic in-patients with anger control problems (n = 31) show more mood variability than student controls (n =31).
2. To determine the relationship between anger variability and measures of anger and personality

Method

Forensic in-patients completed a diagnostic interview (MINI). Subjects used visual analog scales twice a day for 7 days to record 4 moods (angry, tense, depressed, high moods). Also completed were the STAXI Anger Expression Inventory, TEMPS-A and the NEO-FFI for anger, temperament and personality assessment respectively.

Results

4 TEMPS subscales (depressed, anxiety, cyclothymia, irritability) and the STAXI state and anger control index were higher in patients than controls. The VAS derived mean square successive difference (composite measure of variability) and SE for tense, angry and depressed moods were higher in patients. Anger variability was significantly correlated to the Anger Expression index of the STAXI- II but not to STAXI state anger, TEMPS irritability nor NEOFFI agreeableness.

Conclusion

Patients with anger problems show higher variability of anger, tension and depression. Anger in these patients is variable rather than trait-like, and reactive to situations. This has treatment implications.

References:

1. Bowen RC, Clark M, Bates M: Mood swings in patients with anxiety disorders compared with normal controls. J Affec Disord 2004; 78: 185-192.
2. Oosterwegel A, Field N, Hart D, Anderson k: The relation of self esteem variability with emotion variability, mood, personality traits and depressive features. J Pers 2001; 69 (5): 689.

NR756 Wednesday, May 24, 3:00 PM - 5:00 PM

911 Calls at Methadone Clinics, Convenience Stores, and Residences

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Educational Objectives:

1. To understand the bases of community opposition to methadone treatment clinics.
2. To know the relationship between methadone treatment clinics and measures of criminal activity in their neighborhoods.

Summary:

Introduction: Community resistance to methadone treatment clinics stems largely from fear about crime, although there is very little empirical data regarding the geographical relationship between methadone clinics and crime. We addressed this issue by mapping 911 calls to police around 11 methadone clinics and 11 matched convenience stores and residential points in Baltimore, MD between Jan. 1, 1998 and Dec. 31, 2001. **Methods:** Sites and 911 calls were geocoded (mapped) by street address. Concentric circular "buffers" were drawn at 25, 50, 75, and 100 meters around each site, and the calls per unit area calculated. Linear regression was used calculate the "crime slope" (parameter estimate = β), comparing the crimes per area among the buffers, with a negative slope indicating more crimes closer to the site. **Results:** Total calls increased closer to the clinics (β = -0.0226, p<.0001) and

convenience stores (β = - 0.0202, p <0.01), but decreased closer to residences (β= 0.0102, p <0.0001). Similar results were found for violent and financial calls. Drug calls did not significantly increase closer to methadone clinics (β= -0.0175, p < 0.2795), but increased closer to convenience stores (β= -0.0292, p < 0.0007) and decreased closer to residences (β = 0.0139, p <0.0009). There was no difference in calls (crime slopes) between clinics and convenience stores, but clinics had more calls residential points. **Conclusion:** These findings suggest that the increased 911 calls closer to methadone clinics are similar to that around other high-density foot-traffic sites such as convenience stores and are not drug-related.

Supported by the Substance Abuse Policy Research Program of the Robert Wood Johnson Foundation and the Intramural Research Program of the National Institutes of Health, National Institute on Drug Abuse and the Center for Substance Abuse Treatment of the Substance Abuse and Mental Health Services Administration.

References:

1. Cadiz L, Kay LF. Following addicts, methadone debate migrates to suburbs: Neighbors fearing worst fight clinics in Maryland. Baltimore Sun 2003 Aug 18; Sect. A:1-3.
2. Rich TF. The use of computerized mapping in crime control and prevention programs. Research In Action, 1-11. 1995. National Insititute of Justice, Office of Justice Programs, U.S. Department of Justice.

NR757 Wednesday, May 24, 3:00 PM - 5:00 PM

Survey Evaluation of the Abuse Potential of Short-Acting Versus Long-Acting Stimulants in ADHD

George M. Bright, M.D. *Adolescent Health Center, 13821 Village Mill Drive, Ste B, Midlothian, VA, 23114*

Educational Objectives:

At the conclusion of this session, participants should be able to describe the abuse potential of stimulants used to treat attention-deficit/hyperactivity disorder and recognize the greater likelihood of abuse with short-acting vs. long-acting stimulants.

Summary:

Introduction: Research has suggested that the abuse potential of immediate-release stimulants is greater than that of extended-release stimulants. Subjects receiving treatment for ADHD were surveyed to assess the abuse potential of other commonly used short-acting and long-acting stimulant medications.

Methods: We report here an interim analysis of an ongoing survey intended to be distributed to nearly 1000 respondents enrolled in an ADHD treatment center. In addition to demographic questions, general questions about illicit drug use and misuse of prescribed stimulant medication, respondents were polled about the type of stimulant medication most frequently misused or abused (short-acting or long-acting) and how the stimulant was prepared and administered (crushed and inhaled, crushed and injected, soaked overnight in water and injected or consumed orally, heated in a microwave to melt down and inject, drink, or snort).

Results: A total of 40 surveys have been returned to date. Fifty percent of the respondents were 18 to 25 years of age and nearly 50% of them began taking stimulants between the ages of 6 and 17. Four (10%) of the respondents reported stimulant misuse/abuse —3 (75%) with short-acting stimulants and 1 (25%) with a long-acting stimulant. All stimulants were crushed and inhaled.

Conclusions: In this interim analysis of survey data, short-acting stimulants were involved to a greater extent than long-acting stimulants for subjects who reported stimulant misuse/abuse. This suggests a relative benefit of long-acting agents in ensuring appropriate stimulant use and decreased stimulant misuse/diversion.

This study was funded by Shire Pharmaceuticals Inc.

References:

1. Foltin RW, Fischman MW. Assessment of abuse liability of stimulant drugs in humans: a methodological survey. Drug Alcohol Depend. 1991;28:3-48.
2. Kollins SH, et al. Comparison of acute behavioral effects of sustained-release and immediate-release methylphenidate. Exp Clin Psychopharmacol. 1998;6:367-374.

NR758 Wednesday, May 24, 3:00 PM - 5:00 PM

Lost Work Days and Emergency Department Visits Among Patients Treated for Bipolar Disorder

Richard Alan Brook, M.S. *The JeSTARx Group, Retrospective Analysis, 18 Hirth Drive, Newfoundland, NJ, 07435-1710*, Krithika Rajagopalan, Ph.D., Suzanne Novak, M.D., Nathan Kleinman, Ph.D., James E. Smeeding, R.Ph., Harold H. Gardner, M.D.

Educational Objectives:

At the conclusion of the session, the participant should be able to compare the differences in annual lost workdays and ED visits among patients with bipolar disorder treated with different classes of psychotropic drugs.

Summary:

Summary:

Objective: To evaluate total lost days (TLDs) and mental health-related emergency department (ED) visits for patients with bipolar disorder (BPD) treated with different classes of psychotropic drugs.

Methods: Analysis of TLDs and ED visits for 1,211 patients with BPD from a database of 300,000 United States employees and their spouses (2001-2004). Patients were classified into three treatment cohorts (those on atypical antipsychotics only [ATYP]; those on conventional antipsychotics and/or mood stabilizers only [OTHER]; and those using medications from both categories [BOTH]) and one control cohort (those using no study-specified psychotropic medications [NONE]). Controlled regression models compared TLDs and percentage of patients with mental health-related ED visits between cohorts during the year following an index prescription (an average date was used for the control group). Only employees eligible for work-absence benefits were included in comparisons of TLDs.

Results: Overall, the number of patients classified into the ATYP, OTHER, NONE, and BOTH cohorts were 51, 522, 272, and 366, respectively. Mean TLDs were least for the ATYP cohort (6.3 days, 4 patients), followed by OTHER (12.4 days, 72 patients), NONE (30.3 days, 30 patients), and BOTH (35.3 days, 30 patients) treatment cohorts. TLDs were significantly lower with ATYP than OTHER and NONE ($P<0.05$). The percentage of patients with an ED visit was lowest for the ATYP cohort (0.25%, 51 patients), followed by the OTHER (1.57%, 522 patients), NONE (2.17%, 272 patients), and BOTH (5.11%, 366 patients) treatment cohorts. The ATYP and OTHER groups demonstrated significantly lower percentages of patients with ED visits than the BOTH group ($P<0.05$).

Conclusion: Patients with BPD treated only with atypical antipsychotics reported fewer work absences and were less likely to have mental health-related ED visits than other treated and untreated cohorts.

Supported by funding from AstraZeneca Pharmaceuticals LP.

References:

1. Bryant-Comstock, L., Stender, M., Devercelli, G. (2002) Health care utilization and costs among privately insured patients with bipolar I disorder. Bipolar Disord 4:398-405.

2. Kleinman, N.L., Brook, R.A., Rajagopalan, K., Gardner, H.H., Brizee, T.J., Smeeding, J.E. (2005) Lost time, absence costs, and reduced productivity output for employees with bipolar disorder. J Occup Environ Med 47:1117-1124.

NR759 Wednesday, May 24, 3:00 PM - 5:00 PM

An Item Analysis of the Beck Depression Inventory to Assess Symptoms of Perinatal Depression

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize how the Beck Depression Inventory can be used with pregnant and postpartum women.

Summary:

Objective. The overlap of the typical symptoms of pregnancy with those of depression dictates that depression rating instruments such as the Beck Depression Inventory (BDI) be subjected to validation in that clinical context. Furthermore, a brief screening instrument, based on the Beck Depression Inventory (BDI), to assess depression in pregnant and postpartum women, would be a welcome tool for busy obstetrical practitioners.

Method. Beck Depression Inventory and Clinical Global Impressions (CGI) data were collected on 354 pregnant and postpartum women. The results were grouped into five categories (first trimester, second trimester, and third trimester, as well as 0-6 weeks postpartum and 6-52 weeks postpartum). The data was analyzed groupwise to determine if differences existed between BDI items across groups.

Results. All items of the BDI correlated significantly with the total score, confirming internal consistency. Item-total score correlation coefficients ranged from 0.344 to 0.828 across groups. Cronbach alpha coefficients ranged from 0.91 to 0.94. Receiver operator characteristic curves were drawn to determine BDI total score cutoffs. In all five groups, a BDI score of 14 was selected to give an average sensitivity and specificity of 0.74 and 0.81, respectively. Item analysis showed that BDI items of sadness, pessimism, loss of pleasure, self-dislike, and loss of interest correlated with BDI scores across groups. Full and abbreviated scales correlated significantly across all groups ($r > 0.9$, $p = 0.01$).

Conclusion. The Beck Depression Inventory and a five-item quick screening subscale are valid for use during pregnancy and postpartum. This subscale may be used in women's health offices as an expeditious yet reliable means to assess perinatal depression.

References:

1. Beck AT, Steer, RA, Garbin, MG: Psychometric properties of the Beck Depression Inventory: Twenty-five years of evaluation. Clin Psych Review 1988; 8: 77'100.

2. Beach, AJ, Henry, AL, Newport, DJ, Stowe, ZN: The fetus and maternal depression: Implications for antenatal treatment guidelines. Clin Obstet & Gyn 2004; 47: 535-546.

NR760 Wednesday, May 24, 3:00 PM - 5:00 PM

Suicidality in Treatment-Resistant Depression: Results From a 24-Month Trial of Vagus Nerve Stimulation

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Educational Objectives:

To present data on suicidality in persons with treatment resistant depression during 24 months of therapy with vagus nerve stimulation therapy.

Summary:

Objective- Depression is a risk factor for eventual suicide and recent attention has focused on the possibility that treatment with antidepressants may contribute to that risk. This paper addresses the effect of a newly approved therapy for treatment-resistant depression, vagus nerve stimulation (VNS) therapy, on suicidality over a 24- month period in persons with treatment-resistant depression.

Method- This analysis describes the suicides, attempted suicides, suicidal ideation, and hospitalizations for worsening depression that were documented each quarter during the first 24 months of the pivotal study of VNS for treatment-resistant depression.

Results- 235 subjects enrolled and 205 participants received >3 months of VNS therapy. One of the 235 participants committed suicide (rate of 0.27% suicide/patient year) and eight participants made 10 suicide attempts. Suicide attempts and hospitalizations for worsening depression peaked in the second quarter of stimulation and declined thereafter. Study participants were most likely to endorse suicidal ideation or intent at baseline and the number doing so declined at subsequent visits. Responders to VNS therapy had significantly lower ratings on the rated suicide items at each interval.

Conclusions- Suicidality generally declined during 24 months of stimulation in this group with treatment-resistant depression, particularly in those who responded to treatment.

References:

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2. Oquendo MA, Malone KM, Mann JJ: Suicide: risk factors and prevention in refractory major depression. Depress Anxiety 1997; 5:202-11.

NR761 Wednesday, May 24, 3:00 PM - 5:00 PM

Adverse Impact of Involuntary Hospitalization on Perceptions of Psychiatric Care in Veterans With Severe Mental Illness

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Educational Objectives:

At the conclusion of this presentation, the participant should learn about the relationship of involuntary commitment on perceptions of care. Because satisfaction is often used as a performance monitor when assessed nationally by the VA, the influence of involuntary commitment on satisfaction measures should be considered when comparing across inpatient providers.

Summary:

Objective: The VA assesses satisfaction with inpatient psychiatric care as a performance monitor. Coercive interventions such as involuntary commitment may impact on patients' perceptions of mental health treatment, yet no studies examined these issues in veterans. Thus, we examined the impact of involuntary commitment and perceived coercion on perceptions of care in veterans with SMI.

Method: Veterans (N=211) with SMI who were psychiatrically hospitalized between March 2004-August 2005 were enrolled. Perceptions of care were assessed using the Perception of Care (POC) survey (global evaluation domain) and involuntary commitment was assessed by record review. Perceived coercion was measured using the Admission Experience Survey. Variables significant at p<0.10 were retained for inclusion in a multiple linear regression model.

Results: Eighty-eight percent of the sample were men, mean age was 50.26, and 34.1% were Caucasian. As to primary psychiatric diagnosis, 50.7% had PTSD, 31.8% had psychotic disorders, and 17.5% had mood disorders. Nearly seventeen percent (n= 35) were involuntarily committed and 67.3% perceived some coercion at the current psychiatric hospital admission. Forty-five percent had a lifetime involuntary commitment history and 30.5% reported they were denied a needed medication during a hospitalization. The mean global POC score was 68.9 (SD=25.2). In the multiple linear regression model controlling for demographics, psychiatric diagnosis, substance abuse, and self-rated health, those who were involuntarily committed or perceived coercion had lower POC scores (b=-13.41; 95% CI=-22.37 to -4.44; p=0.004 and b= -6.58; 95% CI= -13.67 to 0.51; p=0.07 respectively). Subjects who felt they were denied a needed medication had lower POC scores b=-13.67; 95% CI=-20.86 to -6.47; p= 0.0002).

Conclusions: These results suggest that involuntary commitment status and having been denied a medication are significantly related to negative global perceptions of care among psychiatrically hospitalized veterans with SMI. Other variables were not significant in the adjusted model.

References:

1. Swartz MS, Wagner HR, Swanson JW, Hiday VA, Burns BJ: The perceived coerciveness of involuntary outpatient commitment: Findings from an Experimental Study. J Am Acad Psychiatry Law 2002; 30:207-217.
2. Swanson JW, Swartz MS, Hannon MJ, Elbogen EB, Wagner HR, McCauley BJ, Butterfield MI. Psychiatric Advance Directives: A Survey of Persons with schizophrenia, family members, and treatment providers. Int J Forensic Ment Health; 2:73-86.

NR762 Wednesday, May 24, 3:00 PM - 5:00 PM

Does a History of Substance Abuse Predict the Number of Medicines to Which a Fetus is Exposed?

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the impact of having a history of comorbidity with a substance use disorder on maternal behavior in pregnancy.

Summary:

Previous investigations of obstetrical outcome related to medication exposure and/or psychiatric illness have failed to account for other ancillary exposures. A seminal concern, germane to clinical data and treatment guidelines are the factors predicting medication exposures. We hypothesized that women with a mood or anxiety disorder and past history of substance abuse would have more prenatal exposures.

245 pregnant subjects with a mood and/or anxiety disorder were followed prospectively throughout pregnancy to obtain data on maternal drug consumption. Of these, 6 fulfilled SCID criteria for a current substance disorder, and 71 (29%) had a prior history (41 alcohol, 30 drug and alcohol). To test our hypothesis, medication exposures and obstetrical outcome was compared between the three groups.

ANOVA showed significant differences with regard to gynecological medicines (F=5.647, *p<.01*), habit-forming medicines such as alcohol, tobacco, and caffeine (F=4.684, *p<.01*), and the total number of medicines (F=3.108, *p< .05*). Post-hoc analyses confirmed that women with a history of alcohol abuse alone used significantly more gynecological medicines than did women with no history of substance abuse and women with a history of both drug and alcohol abuse (0.22 versus .05 and .03, *p<.01*). Furthermore, women with a history of alcohol abuse alone also used significantly more habit-forming medicines (.76 versus .39, *p<.01*) and more total medicines (5.24 versus 3.74, *p<.01*) than women with no history of drug or alcohol abuse. Initial analysis did not identify significant differences in birth weight or apgar scores between the three groups. Further analysis of obstetrical outcome is underway.

These findings suggest that a history of a substance use disorder may be important for determining maternal health behaviors in pregnancy. Such issues have not been included in previous investigations.

Supported by P50 MH 68036

References:

1. Doering PL, Stewart RB: The extent and character of drug consumption during pregnancy. JAMA 1978; 239(9):843-846.
2. Riley EH, Fuentes-Afflick E, Jackson RA, Escobar GJ, Brawarsky P, Schreiber M, Hass JS: Correlates of prescription drug use during pregnancy. Journal of Women's Health 2005; 14(5): 401-409.

NR763 Wednesday, May 24, 3:00 PM - 5:00 PM

Effectiveness of Aripiperazole in Reducing Craving for Opiates

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Educational Objectives:

At the conclusion of this presentation the participant should be able to recognize the role dopamine plays in addiction and the possible mechanism of action of a partial dopamine agonist - aripiperazole in decreasing craving for opiates in individuals who suffer from opiate dependence

Summary:

Objective: The author examined the effectiveness of aripiperazole, a dopamine receptor partial agonist in reducing craving for opiates in individuals with suffering from opiate dependence.

Method: 40 Patients were chosen from a private practice buprenorphine program. Patients with opiate dependence were treated with buprenoprhine. Intensity of craving was rated biweekly on a 7 item craving scale. If the score on the scale did not decrease by at least 20% from baseline by week 4, aripiperazole 5mg/day was added to the buprenorphine. Patients with a history of schizophrenia and bipolar disorder were excluded. The ratings cntinued on a biweekly basis for the next 6months..

Results: There was a 30% average decline in scores on the craving scale in patients who took abilify for 6 months (N=31). 3

patients dropped out of the study and 6 patients relapsed during the course of the study.

Conclusions: Aripiperazole was effective in reducing craving in opiate dependent individuals maintained on buprenorphine during a 6 month study. It's opiate partial agonist activity may be useful in ameliorating craving in addicted individuals. Longer studies with a larger group of sublects are needed to confirm this.

References:

1. O'Brien CP: Anticraving Medications for relapse prevention: A possible new class of psychoactive medications. Am J Psychiatry 2005; 162: 1423-1431.
2. Kalivas PW, Volkow ND: The Neural Basis of Addiction: A Pathology of Motivation and Choice. Am J Psychiatry 2005; 162: 1403 - 1413.

NR764 Wednesday, May 24, 3:00 PM - 5:00 PM

Health Care Contact Before Suicide: A Population-Based Case-Control Study

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Educational Objectives:

This study describe the health care contact before suicide using a national sample and case-control design.

At the conclusion of this presentation, the participant should be able to undertstand the health care contact varied before suicide by sex and age group.

Summary:

Objective:The purpose of this study was to describe the health care contacts before suicide, accidental, and natural deaths.

Method:All the 2,781 suicide cases in Taiwan in 2001 were identified and matched by age levels with accidental and natural deaths using 1:2:3 ratios as the controls. These three groups were linked with National Health Insurance Database.

Results: Suicide cases had more contacts psychiatrists than the subjects dead by accident and natural causes. In the last month before suicide, 49.1 % had consulted non-psychiatric doctors and only 7.4% had consulted psychiatrists. Males and the elderly (aged over 65 years) were the least likely to consult psychiatrists before their suicides.

Conclusion: The majority of individual who commit suicide do not consult psychiatrists before their deaths. The proportion who had had prior contact varied between different age and sex groups and individuals in groups with the higher suicide rates tended to have the least contact.

References:

1. Andersen UA, Andersen M, Rosholm JU, Gram LF: Contacts to the health care system prior to suicide: a comprehensive analysis using registers for general and psychiatric hospital admissions, contacts to general practitioners and practising specialistsi.
2. Evans J: The health service contacts of 87 suicides. psychiatric Bulletin 1994; 18:548-550.

NR765 Wednesday, May 24, 3:00 PM - 5:00 PM

Prescription Pattern of Antipsychotics Under Reimbursement Restriction-Analysis of National Health Insurance Database in Taiwan

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Educational Objectives:

The participants should learn that taking Taiwan's national insurance as an example, the reimbursement restriction may affect the prescription patterns and the access of the patients with schizophrenia to newer treatment.

Summary:

Objective: The increased expenditure of newer antipsychotics is a challenge to the drug benefit programs. Reimbursement restriction is one way to control the cost but has been criticized for potentially preventing some patients from receiving optimal treatment in some studies. The reimbursement of second generation antipsychotics (SGA) had been under restriction by Taiwan National Health Insurance Bureau before 2002. This study was to explore the impact on the prescription patterns of antipsychotics under such restriction in a national representative sample of schizophrenia in Taiwan.

Methods: The nationwide medical claim data of the patients with schizophrenia who had at least one psychiatric inpatient record in Taiwan from 1995 to 2001 were collected. The pharmacy dataset included complete records of inpatient and outpatient prescription from 1997 to 2001.

Results: A total of 49,425 patients (male 57.6%) were enrolled. Mean age was 40 (SD 12.9). The prescription rate of conventional antipsychotic dropped significantly from 97% to 82% between 1997 and 2001. There were significant linear trends of increased rates of treatment with clozapine (from 7.9% to 15%) and other antipsychotics (from 3.4% to 28.8%) from 1997 to 2001. However, the rates of the ECT treatment decreased linearly from 2.0% (1997) to 1.5% (2001) with marginal significance. Regarding the characters of hospitals on the prescription patterns, there was robust growth in medical centers (from 0.7% to 44.3%) compared to other general hospitals (1.5% to 35.2%) and mental hospitals (4 % to 17.4%). These differential findings cannot be explained by disease severity alone.

Conclusions: The reimbursement restriction seemed effective to control the rapid growth of prescription of SGA in Taiwan as compared to that in the USA and Italy. The restriction had some impact on the access of the patients with schizophrenia to newer treatment.

References:

1. Rothbard AB, Kuno E, Foley K: Trends in the rate and type of antipsychotic medications prescribed to persons with schizophrenia. Schizophrenia Bulletin 2003;29:531-40.
2. Trifiro G, Spina E, Brignoli O, Sessa E, Caputi AP, Mazzaglia G: Antipsychotic prescribing pattern among Italian general practitioners: a population-based study during the years 1999-2002. Eur J Clin Pharmacol. 2005; 61:47-53.

NR766 Wednesday, May 24, 3:00 PM - 5:00 PM

Challenges and Strategies for Recruitment of Low-Income, Minority, Postpartum Women

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize challenges to recruiting low-income, minority

women, and will have strategies to employ to improve recruitment into studies of postpartum depression.

Summary:

Introduction: Scientific literature contains few descriptions of challenges and recruitment strategies of low-income, minority, postpartum women.

Objectives: 1) Describe recruitment of low income, minority women into a study of postpartum depression. 2) Describe challenges encountered and strategies used to improve recruitment.

Methods: The original study was designed to validate screening tools for postpartum depression in low-income women across the first postpartum year. Women were approached during well childcare visits in an urban pediatric clinic. Women provided consent, completed the CES-D, and scheduled an appointment for a clinical interview. Non-identifying demographic information was collected from women who declined. At the interview, women received reimbursement for their time. Transportation and on-site childcare were available. Descriptive statistics and bivariate analyses of non-participants and participants were conducted. Descriptions of the challenges and study changes to enhance recruitment are provided.

Results: Of 449 women approached, 91% (N=408) consented to be interviewed. Of these, 48% (N=194) completed the interview with 81% (N=157) coming to their first scheduled appointment. For those completing a rescheduled interview (N=37), staff averaged 2.19 telephone calls per woman. Of those not completing the study (N=214), 64% (N=134) were lost to follow up. For these women, staff averaged 3.91 telephone calls per woman. Two percent (N=3) of women who completed the study and 22% (N= 30) who were lost to follow up missed appointments without notice. Helpful strategies included payment in cash, full time recruiters, and telephone confirmation of appointments.

Conclusions: Recruitment of low-income, minority women into postpartum depression research studies is challenging. Resources may be better spent recruiting more women initially, as few women who did not come to their first appointment completed the study. However, differences between these two groups may exist and must be further evaluated. Women lost to follow-up may reflect a particularly high-risk population that requires more intensive outreach.

References:

1. Miranda J, Chung JY, Green BL, Krupnick J, Siddique J, Revicki DA, Belin T: Treating depression in predominantly low-income young minority women. JAMA 2003; 290:57-65.

2. Peindl KS, Wisner KL: Successful recruitment strategies for women in postpartum mental health trials. Journal of Psychiatric Research 2003; 37:117-125.

NR767 Wednesday, May 24, 3:00 PM - 5:00 PM

An Individualized Design of Long-Term Occupational Rehabilitation of Chronic Schizophrenic Patients in Taiwan: Yu-Li Model

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to demonstrate the importance of the diversity and local significance in occupational rehabilitation individualized for each patient with schizophrenia.

Summary:

Objective: To promote the occupational participation of chronic schizophrenic inpatients in Yu-Li Hospital via thorough, continuous, and multi-disciplinary occupational rehabilitation evidence based model program (Yu-Li Model). **Materials** & **Methods:** We recruited 2300 subjects with confirmed diagnosis of schizophrenia (DSM-IV criteria) from Yu-Li Hospital, Taiwan. Each subject was assigned to a specific occupational program based on their functional rating score. The intervention period lasted from 2 months to 24 months. **Results:** The individual-oriented occupational rehabilitation programs served 2300 subjects during the study period. According to unique characteristics of reserved occupational potency on each individual, participants received evidence-based programs including (1)industrialized rehabilitation with year yield harvests of rice around 350000 kilograms; (2)community based recreations and volunteer service rehabilitation reaching almost 98% satisfactory rate; (3)autonomous administration system with self-governing rehabilitation fully elected by patients themselves. **Conclusions** & **Discussions:** Throughout the diverse, industrialized, self-devoted and community based rehabilitation, programs, it seemed that more chronic schizophrenic patients are satisfied with their life quality. In addition a significant increase on the accessibility of occupational therapy is observed through this Yu-Li model program.

References:

1. Hoge CW, Toboni HE, Messer SC, Bell N, Amoroso P, Orman DT. The occupational burden of mental disorders in theU.S. military: psychiatric hospitalizations, involuntary separations, and disability. Am J Psychiatry. 2005;162(3):585-91.

2. Dooley NR, Hinojosa J. Improving quality of life for persons with Alzheimer's disease and their family caregivers: brief occupational therapy intervention. Am J Occup Ther. 2004;58(5):561-9.

NR768 Wednesday, May 24, 3:00 PM - 5:00 PM

Neuropsychological Impairment in Pedophiles, Opiate- Addicted Subjects, and Healthy Controls

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Educational Objectives:

At the conclusion of the presentation, the participant should be able to understand the similarities and differences in cognitive performance between healthy controls, pedophiles, and methadone-withdrawn former opiate addicts.

Summary:

The question of neuropsychological impairment in pedophilia has received increasing attention of late. Several articles have found evidence of executive function deficits consistent with impairment of impulse control and behavioral inhibition. However other studies have found conflicting data. The current study addresses whether there is evidence of impairment on a wide array of neuropsychological tests and whether such impairment differs from that found in another population characterized by impulsivity. Forty-seven pedophilic subjects recruited from an outpatient facility specializing in the treatment of sex offenders, 27 former opiate addicted subjects in a residential treatment program to detoxify from methadone, and 58 healthy controls recruited from media sources were administered a battery of neuropsychological tests. The three groups differed on the Wisconsin Card Sorting Test, the Stroop Color Word Test and the Matching Familiar Figures Test but did not differ on the Controlled Oral Word association test, Trailmaking A and B, and the Porteus Maze test. On all

significant post-hoc comparisons healthy controls scored better than either patient group. There were no differences between pedophiles and former opiate users and the two groups differed from controls on all the same tests. These findings suggest that both patient groups may suffer from neuropsychological impairment, which may relate to impaired judgment and impulse control.

References:

1. Cohen LJ, Galynker I: Clinical Features of Pedophilia. J Psychiat Practice 2002; 8,5:276-289.
2. Cohen LJ, Nikiforov K, Watras-Gans S, Poznansky O, McGeoch P, Weaver C, Gertmenian-King E, Cullen K Galynker I: Heterosexual male perpetrators of childhood sexual abuse: A preliminary neuropsychiatric model. Psychiat Quart 2002; 73,4:313-335.

NR769 Wednesday, May 24, 3:00 PM - 5:00 PM

Evaluation of Drug-Drug Interactions With Indiplon

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Educational Objectives:

At the conclusion of this session, the participant should understand the drug-drug interaction profile or indiplon

Summary:

Objectives: To characterize the drug-drug interaction profile of indiplon, a Gamma-aminobutyric acid -A potentiating hypnotic that has been shown to be effective in both inducing and maintaining sleep in patients with chronic insomnia. In vitro studies show indiplon is metabolized partly by CYP3A4 and partly by carboxyesterases and is approximately 80% protein bound. Indiplon is not a P-glycoprotein substrate.

Methods: A series of studies in young, healthy volunteers evaluated the potential for clinically relevant pharmacokinetic (PK) interactions between indiplon (up to 30 mg dose) and several other agents.

Results: Indiplon did not alter the PK of warfarin, theophylline or digoxin. The pharmacodynamic effects of warfarin 20 mg (PT, INR) were not altered by indiplon 30 mg. Co-administration of indiplon with antidepressants (sertraline 50 mg/day, paroxetine 20 mg/day, venlafaxine 150 mg/day, amitriptyline 50 mg/day) did not alter indiplon pharmacokinetics and there were no additive effects in tests of psychomotor function or alertness (Digit Symbol Substitution Test, sleepiness VAS). Co-administration of indiplon with olanzapine 5 mg had no effect on the PK of either agent. Indiplon exposure increased by approximately 2.4-fold when administered with the potent CYP3A4 inhibitor, ketoconazole, and by approximately 25% when administered with the moderate CYP3A4 inhibitor, Extended Release ythromycin. Co-administration with the potent CYP3A4 inducer, rifampin, decreased indiplon exposure by approximately 70%. No tolerability concerns were identified in these studies.

Conclusions: No clinically relevant drug-drug interactions were observed in the presence of several antidepressants, an antipsychotic, and agents with narrow therapeutic indices. Clinically relevant changes in indiplon exposure were observed with potent CYP3A4 inhibition and induction, but not with modest CYP3A4 inhibition. No other clinically relevant interactions with inhibitors were observed. The PK interaction profile of indiplon is consistent with in vitro findings.

Supported by funding from Neurocrine Biosciences Inc. and Pfizer Inc.

References:

1. Foster AC et al. In vivo pharmacological characterization of indiplon, a novel pyrazolopyrimidine sedative-hypnotic. J Pharmacol Exp Ther. 2004;311(2):547-59.
2. Neubauer DN. Indiplon: the development of a new hypnotic. Expert Opin Investig Drugs. 2005;14(10):1269-76.

NR770 Wednesday, May 24, 3:00 PM - 5:00 PM

Neonatal Antidepressant Withdrawal Syndrome: Fact or Fiction?

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Educational Objectives:

At the conclusion of this presentation, the participant will have been presented with a critical appraisal of antidepressant withdrawal symptoms utilizing a prospectively obtained data set.

Summary:

Neonatal symptoms potentially associated with maternal antidepressant use proximate to delivery have garnered increased attention over the past 5 years (Kaye & Weinstein, 2005), despite an initial study discussing similar concerns with tricyclic antidepressants (Webster, 1973). Remarkably, some of these reports have gone so far as to recommend antidepressant discontinuation before delivery. These reports are difficult to synthesize given the wide array of potential confounds and variability in timing and measures employed. For example: 1) no confirmation that women actually took the medication; 2) variable timing of neonatal symptom onset from hours to days - raising questions about neonatal medication clearance; 3) no blinded infant assessment; and 4) limited control of other potentially contributory exposures. Two hundred ninety-four women followed prospectively through pregnancy were included in the current investigation. Neonatal outcomes were assessed in 235 women with laboratory confirmed fetal antidepressant exposure (sertraline n=85, fluoxetine n=65, paroxetine n=36, venlafaxine n=25, citalopram n=17, fFluvoxamine maleateamine n=4, escitalopram n=3)and were compared to 31 women who did not take medication and 28 found to be non-compliant (<2 ng/ml) at delivery. In the exposed group, jitteriness was reported in one neonate (0.4%) and respiratory distress in 24 (10.2%). Similarly, 5 of 59 (8.5%) non-exposed infants showed respiratory distress. Of these 5 infants, only one was in the non-compliant group. These results demonstrate that compliance is not 100% even in a study designed to address medication exposure, only 89% in present study. These data do not support the purported motor symptoms described in previous reports. Detailed analysis of the medication exposures, dose dependent effects based on umbilical cord concentrations, and the potential impact of depressive symptoms will be conducted.

Supported by NIH P50 MH68036

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2. Webster PA :Withdrawal symptoms in neonates associated with maternal antidepressant therapy. Lancet 1973; 2(7824): 318-319.

NR771 Wednesday, May 24, 3:00 PM - 5:00 PM

Factors Associated With the Use of Drugs by Medical Students

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Brazil, Evelyn Doering-Silveira, Sr., M.Psy., Monica Di Pietro, Sr., M.D., Paula T. Oliveira, Sr., M.Psy., Leonardo Q. Rosa-Oliveira, Sr., M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the importance of collecting specific information concerning substance use among medical students.

The audience should also be able to distinguish different patterns of substance use and their respective relevance. Yet, participants should be able to identify risk factors for substance misuse among college students.

Summary:

Recent use of alcohol, tobacco, tranquillizers, amphetamines, cannabis, organic solvents, and cocaine among 456 medical students was surveyed by way of a self-report questionnaire proposed by the WHO (SMART, 1980). Among medical students, after alcohol and tobacco, cannabis and solvents are the most frequently used psychoactive substances (16.2 % and 18.2 %, respectively). As such, they were the most deeply analysed drugs in this study. Factors associated with the recent use of cannabis and solvents were established by logistic regression. Living with parents or a companion appeared as a protective factor for the use of cannabis. However, being male and attending the Sports Centre regularly showed as risk factors for the use of both cannabis and solvents. Concepts and misconceptions concerning protective and risk factors must be discussed in the light of cultural and circumstantial interferences. Harm reduction strategies should be seriously considered.

References:

1. Newbury-Birch D; White M; Kamali F. Factors influencing alcohol and illicit drug use amongst medical students. Drug and Alcohol Dependence 59: 125-130, 2000.
2. Akvardar Y; Demiral Y; Ergör G; Ergör A; Bilici M; Özer AO. Substance use in a sample of Turkish medical students. Drug and Alcohol Dependence 72: 117-121, 2003.

NR772 Wednesday, May 24, 3:00 PM - 5:00 PM

Mental Status of Adolescents Using Ayahuasca Within a Ritual Context

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize differences in the frequencies of psychiatric symptoms among adolescents using hallucinogens n a ritual context.

Summary:

Introduction: Ayahuasca is believed to be harmless for those including adolescents drinking it within a religious setting. Nevertheless controlled studies on the mental/ psychiatric status of ritual hallucinogenic ayahuasca concoction consumers are still lacking. Objective: Forty adolescents from a Brazilian ayahuasca sect were compared with 40 controls matched on sex, age, and educational background for psychiatric symptomatology. Screening scales for depression, anxiety, alcohol consumption patterns (abuse), attentional problems, and BDDs were used. Results: Comparatively to controls, considerable lower frequencies of positive scoring for anxiety (59.1% and 71.4%), body dismorphism (16.7% and 55.6%), and attentional problems (4.1% and 27.3%) were detected among ayahuasca-using adolescents despite overall similar psychopathological profiles displayed by both study groups. Conclusion: Low frequencies of psychiatric symptoms detected among adolescents consuming ayahuasca within a religious context may reflect a protective effect due to their religious affiliation. However further studies on the possible interference of other variables in the outcome are necessary.

References:

1. Callaway JC, McKenna DJ, Grob CS, Brito GS, Raymon LP, Poland RE, Andrade EN, Mash DC - Pharmacokinetics of Hoasca alkaloids in healthy humans, Journal of Ethnopharmacology 65:243-256 (1999).
2. Grob CS, McKenna DJ, Callaway JC, Brito GS, Neves ES, Oberlander G, Saide OL, Labigalini E, Tacla C, Miranda CT,Strassman RJ, Boone KB ' Human psychopharmacology of Hoasca, a plant hallucinogen used in ritual context in Brazil. Journal of Nervous and.

NR773 Wednesday, May 24, 3:00 PM - 5:00 PM

Therapeutic Effects of Long-Term Therapy With Ramelteon in Adults With Chronic Insomnia

Michael DeMicco *Advanced Clinical Research Institute, 1211 West LaPalma Ave, Anaheim, CA, 92801*, Sherry Wang-Weigand, Jeffrey Zhang

Educational Objectives:

At the conclusion of this presentation, the participant should be able to describe the efficacy of long-term ramelteon treatment in adult and older adult subjects with chronic insomnia.

Summary:

Introduction: The long-term safety and efficacy of the chronohypnotic ramelteon, a highly selective MT_1/MT_2-receptor agonist, was evaluated in adults with chronic insomnia.

Methods: Subjects (N=1213) diagnosed with primary insomnia (DSM-IV-TR™ criteria) and reporting symptoms for at least 3 months received ramelteon nightly for 1 year followed by a 3-day single-blind placebo run-out. Subjects 65 years or older received ramelteon 8mg (n=248); those 18 to 64 years received ramelteon 16mg (n=965). Safety was assessed at monthly clinic visits over the course of the study. Efficacy was evaluated by subject-maintained daily sleep diaries and Clinical Global Impression (CGI) assessments performed by the investigator.

Results: Baseline sleep latency was 85.1 and 88.8 min in the 8mg and 16mg groups, respectively; baseline total sleep time (TST) was 293.8 and 304.1 min, respectively. At Month 1, sleep latency significantly improved from baseline with ramelteon 8mg and 16mg by 34.0% and 35.1%, respectively, and continued to improve through Month 6 (44.7% and 49.1%) and Month 12 (50.3% and 52.1%). Considerable improvements in TST were also reported with ramelteon 8mg and 16mg at Month 1 (15.2% and 16.9%), Month 6 (21.6% and 22.7%), and Month 12 (25.5% and 23.9%). No notable changes in sleep latency were reported during the placebo run-out. At 6 months and 1 year, CGI indices showed an improved insomnia condition, a moderate and sustained decrease in severity of illness, and a moderate therapeutic effect. Adverse events in both groups were primarily mild or moderate, low in frequency, and consistent with those reported in previous studies.

Conclusion: Long-term ramelteon treatment improved sleep latency, TST, and CGI in adults. These improvements were sustained throughout 1 year of treatment. Additionally, ramelteon was well tolerated and did not produce rebound insomnia during placebo run-out.

References:

1. Kato K, Hirai K, Nishiyama K, et al: Neurochemical properties of ramelteon (TAK-375), a selective MT1/MT2 receptor agonist. Neuropharmacology 2005; 48:301-310.
2. Zammit G, Roth T, Erman M, Sainati S, Weigand S, Zhang J: Double-blind, placebo-controlled polysomnography and outpatient trial to evaluate the efficacy and safety of ramelteon in adult patients with chronic insomnia [abstract]. Sleep. 2005; 28:A22.

NR774 Wednesday, May 24, 3:00 PM - 5:00 PM

Convergence of In Vitro, Animal, and Human Data to Predict Determinants of Sertraline Serum Concentrations in Depressed Pregnant Women

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to i) discuss the potential clinical significance of sertraline and other psychoactive drugs as substrates of endogenous drug transporters; ii) recognize determinants of placental drug transport; and iii) discuss genetic factors that influence fetal drug exposure from psychoactive drugs.

Summary:

Among the aims of the Specialized Center of Research on Sex and Gender Factors Affecting Women's Health (SCOR) at the Emory University Women's Mental Health Program is the ability to predict antidepressant serum concentrations during pregnancy from a patient's demographic, environmental, and genetic data. In this study, we sought to define the status of sertraline, a commonly used antidepressant during pregnancy, as a substrate for the drug transporter, P-glycoprotein (P-gp), using an ATPase assay and Caco-2 and MDR-1 cell cultures over expressing P-gp. Furthermore, we conducted a pharmacokinetic study in rats to further evaluate sertraline as a P-gp inhibitor. The SCOR database was searched and 26 patients were identified who had been or were receiving sertraline during their pregnancy with multiple maternal serum collections. For these women, 179 serum concentration measures of sertraline were available as well as the genotype for 3 common P-gp gene polymorphisms. The results of the in vitro and animal studies revealed that sertraline is both a substrate and inhibitor of P-gp. These findings converge in population pharmacokinetic modeling of the SCOR patient data confirming that maternal sertraline concentrations correlated with 3435 T allele carriers. P-gp polymorphisms may affect the penetration of sertraline and other substrates across the placenta. The impact of these polymorphisms and others for a variety of medications on fetal exposure is discussed in a separate abstract. The utility of data from a variety of sources to determine the relative clearance and fetal exposure to medications will be tested as additional analysis is pending. The value in predicting maternal serum concentrations and fetal exposure has significant clinical implications in the development of therapeutic monitoring guidelines and the interpretation of any dose dependent effects on outcome.

Supported by NIH P50 MH68036 and R01 MH071811.

References:

1. Tanabe M, Ieiri I, Nagata N, et al. Expression of P-glycoprotein in human placenta: relation to genetic polymorphism of the multidrug resistance (MDR)-1 gene. J Pharmacol Exp Ther 2001;297:1137-43.
2. Wisner KL, Zarin D, Holmboe E, et al. Risk-benefit decision making for treatment of depression during pregnancy. Am J Psychiatry 2000;157:1933-40.

NR775 Wednesday, May 24, 3:00 PM - 5:00 PM

Ropinirole Treatment of Restless Legs Syndrome (RLS) Improves Daytime Functioning and Quality of Life

Karl Doghramji, M.D. *Thomas Jefferson University, 1015 Walnut Street, Suite 319, Philadelphia, PA, 19107*, Michael O. Calloway, Ph.D.

Educational Objectives:

At the conclusion of this session, the participants should be able to describe the negative impact of Restless Legs Syndrome (RLS) on quality of life and daily activities, and the beneficial effects of treatment with ropinirole, a dopamine agonist, on these variables compared with placebo in patients with moderate-to-severe primary RLS.

Summary:

Introduction: The symptoms of Restless Legs Syndrome (RLS) often impact negatively on patients' daily functioning and quality of life (QoL).[1,2] Treatment of RLS symptoms may also provide improvements in daily functioning and QoL, providing substantial benefit to patients' lives.

Methods: A *post-hoc* analysis, using data from three 12-week studies, TREAT RLS 1, 2, and US (protocols: 101468/190, 194, and 249, respectively), investigated the effects of ropinirole on RLS symptoms, daytime functioning, and QoL in patients with RLS. Across the three studies, 465 patients were randomized to ropinirole and 469 to placebo. The primary endpoint was the change from baseline in the International Restless Legs Scale (IRLS) total score at Week 12 last observation carried forward (LOCF). The validated RLSQoL questionnaire was used to measure QoL, and effect on daytime functioning was assessed using Item 9 on the IRLS: "In the past week overall, how severe was the impact of your RLS symptoms on your ability to carry out your daily affairs?" ("none" to "very severe" [0-4]).

Results: Compared with placebo, ropinirole treatment was associated with statistically significantly greater improvements from baseline in IRLS (adjusted mean treatment difference [AMTD]: -3.2; 95%CI: -4.3, -2.1; $p<0.001$) and RLSQoL questionnaire total scores (AMTD: 4.6; 95%CI: 2.6, 6.7; $p<0.001$) at Week 12 LOCF. There was also a significant treatment effect for the distribution of responses to Item 9 on the IRLS at Week 12 LOCF for all patients ($p<0.001$) and for the subgroup reporting at least a moderate impact on this item at baseline (ropinirole, n=203; placebo, n=209; $p=0.020$). In both cases, more patients reported no impact in the ropinirole group compared with placebo.

Conclusions: Ropinirole improved RLS symptoms compared with placebo, and provided enhanced overall quality of life and better daytime functioning.

Study Supported By: GlaxoSmithKline R&D.

References:

1. Trenkwalder C et al. J Neurol Neurosurg Psychiatry 2004; 75: 92-7.
2. Walters AS et al. Mov Disord 2004; 19: 1414-23.

NR776 Wednesday, May 24, 3:00 PM - 5:00 PM

Effect of Ropinirole on Aspects of Sexual Activity in Patients With Restless Legs Syndrome

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Educational Objectives:

At the conclusion of this session, the participant should be able to understand the effect of ropinirole treatment on the impact that Restless Legs Syndrome (RLS) has on aspects of patient's sexual activity.

Summary:

Introduction: RLS is a chronic neurological disorder, characterized by an irresistible urge to move the legs. RLS has been associated with negative health states such as depressed mood[1,2] and reduced libido.[2] This analysis examined the effect of ropinirole on sexual desire and function in patients with moderate-to-severe primary RLS.

Methods: Data were pooled from three double-blind, placebo-controlled trials (protocols: 101468/190, 194, 249). Patients (n= 934) were randomized to receive ropinirole, 0.25-4.0mg titrated as needed and tolerated, once daily 1-3 hours before bedtime, or placebo for 12 weeks. Sexual activity was assessed *post-hoc* using patient responses to questions about sexual desire (Q11; level of interest in sexual activity) and sexual functioning (Q12; level of disturbance or reduction in sexual activities) from the RLS Quality of Life (RLSQoL) questionnaire (rated 'none'-'a lot' [1-5]).

Results: Overall, 930 patients (ropinirole=464, placebo=466) were included in intention-to-treat population; 59% of the ropinirole group and 64% of the placebo group were women, and the mean (SD) ages were 53.5 (11.8) and 54.5 (12.2) years, respectively. At Week 12, responses to the sexual desire item (Q11) were essentially unchanged from baseline and similar between treatment groups (p=0.942). Of those who answered, 22% (87/397) of ropinirole-treated and 21% (86/402) of placebo-treated patients reported "no interest" in sexual activity, compared with 22% (92/419) and 24% (102/419), respectively, at baseline. However, there was a statistically significant treatment difference in favor of ropinirole in responses to the sexual functioning item (Q12) at Week 12 (p=0.004). Significantly more ropinirole-treated patients reported "no disturbance/reduction" in sexual activities due to RLS compared with placebo (294/396 [74%] versus 274/401 [68%]; odds ratio:1.4; 95%CI: 1.0, 1.9).

Conclusions: Ropinirole compared with placebo treatment lessened the adverse impact of RLS on sexual functioning, but did not affect interest in sexual activity.

Study Supported By: GlaxoSmithKline R&D.

References:

1. Hening W, et al. Sleep Med 2004; 5: 237'46.
2. Ulfberg, et al. Mov Disord 2001; 16: 1159'1163.

NR777 Wednesday, May 24, 3:00 PM - 5:00 PM

Buopropion for Methamphetamine Dependence

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Educational Objectives:

At the end of the presentation clinicians should be knowldegable about the effect of Buopropion in the treatemnt of methamphetamine dependence.

Summary:

Methamphetamine dependence is a major public health problem for which there is no effective medication. Buopropion an antidepressant with dopamine realeasing property and mild stimulant effect was studied in a double blind placebo controlled trial in methamphetamine dependent patients. 150 patients with DSM IV diagnosis of methaphetamine dependence were randomized to either placebo or Buopropion 150mg Sustained Release BID. All patients received group psychotherapy (matrix) and were required to come three times a week to the clinic for assessments and urine collections. The primary outcome measure was mean weekly urine. GEE analysis of urine samples showed a trend for efficcacy for buopropion versus placebo (p=0.09). when the group was split into high users and low/moderte users based on baseline use as asessed by TLFB, and using a cut off of 18 days of us in the last 30 days. The group with mild to modeate use (n=71) showed significan effect comarped to teh high user group (p= 0.03). this data suggest that buopropion is efficacious as a pharmacological treatment for mild to moderate methaphetamine dependent patients. A replication study will be neede to confirm this positive finding.

References:

1. Vocci FJ, Elkashef AM: pharmacotherpy and other treatments for cocaine abuse and dependence. Current opinion in psychiatry 2005, 18:265-270.
2. Volkow ND, Wand GJ:Blockade of striatal dopamine transporters by methylphenidate is not sufficient to induce self-reports of high. J pharmacol exp ther 288, 14-20.

NR778 Wednesday, May 24, 3:00 PM - 5:00 PM

Validation of Risk Assessment Tools for Individuals With Problematic Sexual Behaviour and Developmental Delay: Preliminary Results

Paul Fedoroff, M.D. *University of Ottawa Institute of Mental Health Research, Forensic Research Unit, Royal Ottawa Hospital, 1145 Carling Avenue, Ottawa, ON, K1Z 7K4, Canada*, Susan D. Curry, B.A., Gina Madrigrano, Ph.D., Chanie Cunningham, B.A., Athanassia Korovessis, B.A., John M. Bradford, M.B., Deborah Richards, B.A.

Educational Objectives:

At the conclusion of this presentation, the participant should become aware of the issues surrounding the validity of current actuarial risk assessment scales being used to assess intellectually delayed populations and the utility of dynamic risk factors in predicting short term recidivism.

Summary:

Men with developmental delay are over-represented in the criminal justice system and under-represented in correctional treatment programs that are usually designed for the general population of offenders (Griffiths, Richards, Fedoroff & Watson, 2002). There is little research on validating risk assessment measures for developmentally delayed sex offenders. The objectives of this ongoing, externally funded study are to determine the predictive validity of the Violence Risk Appraisal Guide (VRAG), the Sex Offender Risk Appraisal Guide (SORAG; Quinsey, Harris, Rice & Cormier, 1998), and the Short Dynamic Risk Scale (SDRS; Quinsey, Book and Skilling, 2004) within a study population consisting of men with developmental delay about whom concerns about aggression or criminal sexual behaviour have arisen. This study is both multidisciplinary and multisite.

To date 70 developmentally delayed sex offenders and their respective care providers have been recruited from the Ottawa and Niagara sites (30 and 40 respectively). Data to score the VRAG and the SORAG were available for 46 participants. SDRS data for 47 participants with at least two month follow-up were also available for analysis. There were no significant correlations between VRAG or SORAG scores and reported "disruptive behaviours" or SDRS scores .The mean SDRS score for those with no reported events was significantly lower than the mean SDRS score from the month prior to a reported event.

Preliminary findings suggest that in this population, the SDRS is a more effective tool than the VRAG or SORAG for prediction of short term "recidivism".

References:

1. Quinsey VL,Harris GT, Rice ME, Cormier CA: Violent Offenders: Appraising and Managing Risk. Washington, DC, American Psychological Association, 1998.
2. Quinsey VL, Book A, Skilling TA: A follow-up of deinstitutionalized men with intellectual disabilities and histories of antisocial behaviour. J Appl Res Intellect Disabil 2004; 17: 243-253.

NR779 Wednesday, May 24, 3:00 PM - 5:00 PM

Comparison of Violence Risk Appraisal Guide and Sex Offender Risk Appraisal Guide Items in a Sample of Developmentally Delayed Sex Offenders and Non Delayed Sex Offenders

Paul Fedoroff, M.D. *University of Ottawa Institute of Mental Health Research, Forensic Research Unit, Royal Ottawa Hospital, 1145 Carling Avenue, Ottawa, ON, K1Z 7K4, Canada*, Susan D. Curry, B.A., Gina D. Madrigrano, Ph.D., Chanie Cunningham, B.A., John M. Bradford, M.B.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the possible problems associated with using the Violence Risk Appraisal Guide and the Sex Offender Risk Appraisal Guide with the intellectually/developmentally delayed.

Summary:

Accurate prediction of whether an offender will commit subsequent acts of violence or sexual aggression has been a primary concern in forensic research. Over the course of the past 20 years, extensive research has been conducted to assess the validity and effectiveness of various risk appraisal instruments with sexual and violent offenders. Despite the fact that developmentally delayed populations were not adequately represented in the development of these risk assessment measures, they have nonetheless been used to assess the developmentally delayed. The purpose of this study was to compare the scores of two groups of convicted child molesters on the Sex Offender Risk Appraisal Guide (SORAG) and the Violence Risk Appraisal Guide (VRAG) (Quinsey, Harris, Rice & Cormier, 1998), two widely used risk assessment tools.

Assessment items and total scores on the VRAG and SORAG were compared for thirty-eight developmentally delayed men and 38 without developmental delay. This study did not replicate previous findings (Fedoroff, Selhi, Smolewska, Ng & Bradford, 2001), as no significant differences were found on the total scores between the groups on either the VRAG or the SORAG. However, there were significant differences on a number of the individual scale items.

References:

1. Quinsey VL, Harris GT, Rice ME, Cormier CA; Violent Offenders: Appraising and Managing Risk. Washington, DC, American Psychological Association, 1998.
2. Hare RD: The Hare Psychopathy Checklist-Revised Manual. Toronto, Multi-Health Systems, 1991.

NR780 Wednesday, May 24, 3:00 PM - 5:00 PM

PTSD, Body Mass Index, and Priority Groups in U.S. Military Veterans: The Richmond Experience

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Educational Objectives:

Recognize comorbid obesity in military veterans with Post Traumatic Stress Disorder and relate it to socioeconomic status as defined by Priority Groups

Summary:

Post Traumatic Stress Disorder (PTSD) is associated with co morbid obesity. Body Mass Index (BMI) is a useful parameter to estimate the prevalence of overweight and obesity. In 1996 the US Congress defined eligibility criteria for medical case within the Veterans Administration and defined medical benefits package and Priority Groups based on multiple variables, including low income. The PTSD program database was reviewed. Variables assessed included (1) age, (2) decade of life, (3) height, (4) weight, (5) sex, (6) race, (7) priority groups. We calculated BMI. Of the 252 veterans 167 (66.27%) were in the age range of 50 to 59 years. The mean BMI of all veterans was 30.2 $\pm$ 5.6 kg/m^2. Far exceeding current U.S. population findings, 84.1% of our study population was either overweight or obese. Analysis of variance (ANOVA) revealed decade of life did not predict BMI ($df = 6$, $F = 1.372$, $p = 0.226$). Combining Priority Groups 1& 2 into a single group and Groups 3-6 into a single group revealed that preferred priority grouping was associated with higher BMI. Study suggested that low Socioeconomic status is most likely explanation for greater BMI's in lower priority groups than in higher priority groups. Clearly, more definitive studies are needed with much larger study populations. There was no commercial support funding for this poster presentation.

References:

1. Flegal KM, Carroll MD, Ogden CL, Johnson CL. Prevalence and trends in obesity among US adults, 1999-2000. JAMA 2002;288:1723-7.
2. Magruder KM, Frueh BC, Knapp RG et al. PTSD symptoms, demographic characteristics, and functional status among veterans treated in VA primary care clinics. J Traum Stress 2004;17:293-301.

NR781 Wednesday, May 24, 3:00 PM - 5:00 PM

Psychiatric Symptoms in Children of Depressed Mothers

Rosemarie M. Fritsch, M.D. *Universidad de Chile, Psychiatry, Avda. La Paz 1003 Recoleta, Santiago, 00, Chile*, Maria Elena Montt, Graciela Rojas, M.D., Daniel J. Pilowsky, M.D., Ricardo Araya, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to demonstrate the highly rates of psychiatric symptoms in children of depressed mothers.

Summary:

Depression represents a significant public health concern, especially among poor women. It's associated with disability and it impacts mental health of their children. Treatment programs at primary care clinics don't consider mental health of other members of the patient's family.

Objective:

The aim of the present communication is to describe psychiatric symptomatology among offspring of poor depressed mothers who have consulted in primary care clinics (PCC) in Santiago de Chile.

Method:

Mothers were consecutively assessed for depression with the Mini International Neuropsychiatric Interview (M.I.N.I.) and confirmed by an experienced psychiatrist in 3 PCC in poor quarters.

One child per woman (N=309), aged 6 to 16 years, was selected using an aleatory method by the Kish table. Children's assessments included social and global functioning (Children's Behavior Checklist (CBCL)), Child Depression Inventory (CDI), Brief Psychiatric Rating Scale for Children and Adolescents Reviewed (BPRS-CA-R), Screen for Child Anxiety Related Emotional Disorders (SCARED) and Swanson, Nolan and Pelham Rating Scale-Revised (SNAP-IV). Maternal assessments included the Hamilton Depression Rating Scale (HAM-D).

Results:

Most children (62,4%) had scores high enough to suspect further assessment for anxiety disorders and 15,6% had depressive symptomatology. 12,4% had inattention, hyperactivity/impulsivity 25,6% and 11% oppositional/defiant behavior. A positive correlation was find between anxiety and mother's depression in daughters but not in sons.

Conclusions:

Children of poor depressed consultant mothers appear to have highly rates of psychiatric symptoms in a sample in Santiago de Chile. There is a correlation between psychopathology of the mother and of her daughter but not of her son. These findings suggest that is necessary an offspring's psychiatric assessment of depressed consultants and eventually implementation of treatment programs for them.

References:

1. Lieb R, Isensee B, Hofler M, Pfister H, Wittchen HU. Parental major depression and the risk of depression and other mental disorders in offspring: a prospective-longitudinal community study Arch Gen Psychiatry. 2002 Apr;59(4):365-74.
2. Weissman MM, Wickramaratne P, Nomura Y, Warner V, Verdeli H, Pilowsky DJ, Families at high and low risk for depression: a 3-generation study. Arch Gen Psychiatry. 2005 Jan;62(1):29-36.

NR782 Wednesday, May 24, 3:00 PM - 5:00 PM

Improvement of Clinical Global Measures in Alcohol-Dependent Patients Treated With Acamprosate

Allyson Gage, Ph.D. *Forest Laboratories, Inc., Clinical Development & Medical Affairs, Harborside Financial Center, Plaza V, Jersey City, NJ, 07311*, Sylvie Chabac, M.D., Anita Goodman, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the efficacy of acamprosate in improving overall symptomatology associated with alcohol dependence through clinical global measures.

Summary:

Introduction: Multiple controlled trials have shown that acamprosate in combination with psychosocial support is more effective than placebo in maintaining abstinence in alcohol-dependent patients. This study evaluates acamprosate efficacy in three pivotal trials using clinical global measures.

Methods: Alcohol-dependent patients receiving 1998 mg/day acamprosate (n=348) or placebo (n=375) were evaluated on the Clinical Global Impression (CGI) Severity or Improvement scale (13- and 52-week studies), the investigator's assessment of success/failure (48-week study), or the Patient Global Impression of Improvement (PGI-I) scale (13-week study) at study end. Study retention was also examined.

Results: On the CGI-I, significantly more patients had "marked" or "moderate" improvement with acamprosate versus placebo (13-week: 71% versus 47% and 52-week: 80% versus 61%; p<0.005) and symptoms ratings of "insignificant" or "absent" on the CGI-S (13-week: 60% versus 46%, p=NS; 52-week: 66% versus 48%, p=0.005). On the PGI-I, significantly more patients showed "marked" or "moderate" improvement with acamprosate versus placebo (13-week: 75% versus 61%, p=0.008). The rate of treatment success as determined by the investigators was significantly higher with acamprosate versus placebo (48-week: 43% versus 21%, p=0.001). Treatment with acamprosate was associated with a significantly longer study retention in all three studies (p<0.05 versus placebo).

Conclusions/Discussion: Acamprosate treatment confers meaningful qualitative benefits to alcohol-dependent patients through clinical improvement, reduced symptom severity, and longer study participation.

References:

1. Pelc I, Verbanck P, Le Bon O, Gavrilovic M, Lion K, Lehert P: Efficacy and safety of acamprosate in the treatment of detoxified alcohol-dependent patients. A 90-day placebo-controlled dose-finding study. Br J Psychiatry 1997; 171:73-77.
2. Sass H, Soyka M, Mann K, Zieglgansberger W: Relapse prevention by acamprosate. Results from a placebo-controlled study on alcohol dependence. Arch Gen Psychiatry 1996; 53:673-680.

NR783 Wednesday, May 24, 3:00 PM - 5:00 PM

Adolescent Suicide in Quebec: The Evolution of a Constant Phenomenon

Pierre W. Gagne, M.D. *Sherbrooke University, Psychiatry, 234 Dufferin Ste 300, Sherbrooke, PQ, J1H 4M2, Canada*, Valerie Trottier-Hebert, Marie-Claude Cote, M.D., Todd A. Jenkins, M.S.C.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to:

Identify socio-demographical variables associated with completed suicides in adolescents.

Recognize the main clinical diagnoses associated with completed suicides in adolescents.

Recognize the main personality traits and psychosocial variables associated with completed suicides in adolescents.

Assess the need for screening and treatment of teenagers with identifiable risk factors.

Summary:

Objectives: The Canadian Province of Quebec has one of the highest rates of adolescent suicides in the world. Moreover, it appears that the vast majority of its teenage suicide completers are Canadians of French origin, although the highest incidence is being found in the Inuit (Native Canadians) communities. Adolescent suicide risk factors already recognized in the literature include male gender, mood disorders, previous suicide attempts, poor parent-child communication and substance abuse. However, an alarmingly high proportion of adolescents suffering from mental disorders or bearing evident risk factors for suicide are not receiving treatment. The main goals of this retrospective study were 1) to identify socio-demographical, clinical and psychosocial factors associated with suicide within the Quebec adolescent population, 2) to compare two different cohorts of teenage suicide completers in the Province of Quebec and 3) to provide comprehensive data necessary for the creation and implementation of effective screening programs.

Methods: All (n = 425) files on suicides committed by individuals 19 years and younger in a five-year period (1999-2003) were reviewed at the Quebec Coroner Office. Socio-demographical, clinical and psychosocial variables were used and this new cohort was compared to an older cohort of 355 Quebec adolescent suicide completers between the years 1989 and 1992.

Results: The results will be discussed in light of recommendations for more systematic screening of adolescents with identifiable risk factors as well as more options for effective interventions.

References:

1. Practice parameters for the assessment and treatment of children and adolescents with suicidal behavior. J. Am. Acad. Child Adolesc. Psychiatry, 2004; 40 (7 supplement): 24S-51S.

2. Beautrais, AL.: Suicide and Serious Suicide Attempts in Youth: A Multiple-Group Comparison Study. Am J Psychiatry 2003; 160: 1093-1099.

NR784 Wednesday, May 24, 3:00 PM - 5:00 PM

Differences Between Patients With Rapid Cycling Bipolar I and II Disorders in Comorbid Anxiety Disorder and Substance Use Disorder

Keming Gao, M.D. *Case Western Reserve University, Psychiatry, 11400 Euclid Ave., Cleveland, OH, 44106*, Carla Conroy, B.A., Sarah Bilali, M.A., Steven J. Ganocy, Ph.D., Omar Elhaj, M.D., Joseph R. Calabrese, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the differences between patients with rapid cycling bipolar I and II disorders in comorbid anxiety disorder and substance use disorder.

Summary:

Objective: To study the differences between patients with rapid cycling bipolar I and II disorder (BPI versus BPII) in comorbid anxiety disorder (AD) and substance use disorder (SUD). **Methods:** Data of patients with rapid cycling bipolar disorder in our research studies were analyzed for the differences between patients with BPI and BPII in GAD, panic disorder (PD), and OCD and SUD, dependence or abuse. Diagnoses were ascertained by using the Mini International Neuropsychiatric Interview at the initial assessment. The rates of AD and SUD were compared between patients BPI and BPII. **Results:** of 566 patients, those with BPI (n=320) had significantly higher rates of lifetime GAD (44% versus 24%) and PD (34% versus 20%), but not OCD (8% versus 7%) compared with those with BPII (n=246). Patients with BPI also had significantly higher rates of lifetime history of alcohol (44% versus 23%), cocaine (23% versus 6%), and marijuana dependence (17% versus 5%) than those with BPII. Similarly, patients with BPI had significantly higher rates of recent history of alcohol (24% versus 8%), cocaine (8% versus 4%), and marijuana dependence (8% versus 2%) than their BPII counterparts. However, there were no differences between two groups in the rates of lifetime/recent history of substance abuse including alcohol, cocaine, marijuana, stimulant, sedative, and hallucinogens. **Conclusion:** Significantly higher rates of comorbid AD and SUD in patients with BPI suggest that this group may have more severe symptoms and are more difficult to treat than those with BPII.

References:

1. McElroy SL, Altshuler LL, Suppes, et al. Axis I psychiatric comorbidity and its relationship to historical illness variables in 288 patients with bipolar disorder. Am J Psychiatry 2001; 158: 420-426.

2. Frye MA, Altshuler LL, McElroy SL, et al. Gender differences in prevalence, risk, and clinical correlates of alcoholism comorbidity in bipolar disorder. Am J Psychiatry 2003; 160:883-889.

NR785 Wednesday, May 24, 3:00 PM - 5:00 PM

Differences Between Primary and Secondary Chronic Insomnia in Primary Care

Monica Magarinos, M.D. *Madrid*, Pedro Garcia-Parajua, M.D., Lucia de Ugarte, M.D., Jorge Iglesias, M.D., Luis Caballero, Ph.D., Enrique Baca, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to diagnose chronic insomnia and to learn data about this condition in Primary Care

Summary:

Introduction:
Chronic insomnia (ChI) is a common condition in Primary Care (PC). Regardless that it's often related to psychiatric morbidity it appears to be a strong predictor of future depression and a disabling disorder by itself. The aim of this study was to measure and compare clinical and psychiatric characteristics of both patients with primary ChI and secondary ChI.

Methods:
A random sample of 195 subjects older than 18, from 3 PC Centres of the area of Madrid (Spain) was interviewed using the Oviedo Sleep Questionnaire, a semi-structured interview for sleep disorders. The subjects completed the Patient Health Questionnaire and a recent life changes checklist. Data about medical conditions, drug treatments, days of work lost (last year) and use of health care services (last 3 months), were also collected. Psychiatric and clinical characteristics between groups (primary versus secondary ChI) were compared.

Results:
69 patients fulfilled criteria for ChI and 46 (66,7 %) of them were suffering from any psychiatric disorder (including *subtreshold* conditions). Patients with primary ChI compared to secondary insomnia patients had no significant differences in age, gender, use of health care resources, days of work lost, life events during the last 6 and 12 months. However, patients with secondary ChI compared to primary ChI had more somatic and depressive symptoms (U-Mann-Witney test; p=0,007 and p<0,001, respectively).

Conclusions:
There is an important group of patients among PC attendees suffering primary ChI. Patients suffering primary ChI are comparable to patients with psychiatric disorders and insomnia in terms of days of work lost and use of health care resources.

References:

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2. McCall WV. Sleep in the elderly: burden, diagnosis, and treatment. Prim Care Companion J Clin Psychiatry 2004; 6:9-20.

NR786 Wednesday, May 24, 3:00 PM - 5:00 PM

Barman's Life: Psychosocial Strain in the Catering Business

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that there is psychosocial strain in the catering business and this is assiciated with psychiatric disorders.

Summary:

For many decades people were able to identify with their families and jobs. They knew where they came from and where they belonged.

Globalization and a changing society have deprived some individuals of the network of relationships (Sennett 2000), especially those who showed an undetermined chaotically disorganized attitude towards attachement (Ainsworth 1985, Bowlby 1980). They have increasingly suffered from irritations. Research in psychiatry has shown that these individuals are more likely to develop psychical disorders (personality disorders, addiction). Alfred Adler, who, about a hundred years ago, conducted an inquiry about the tailoring trade, was able to show the relationships between working conditions and health (Kandel 1998). In the same way, we have observed the catering business as an example for various fields of work (Schönberger 1994). We trade video- interviewed psychiatric patients in a withdrawal clinic (cooks, waiters, chambermaids, hotel managers and others) about the psychosocial strain imposed on them by their jobs. All of them felt overburdened, suffering from a lack of free time and recreation. Under these circumstances it was impossible for them to have any private personal relationships. Episodic fits of depression, sleeping disorders, stress (Sapolsky 1995) and somatic diseases were the consequences, so was addiction (alcohol, drugs, gambling). Comorbidity was high and suicidality in connection with identity crises and crises due to a lack of purpose was remarkable.

Further inquiries concerning psychosocial stressors in jobs should be conducted, which would enable us to analyze the factors of vulnerability, as well as protective and preventive aspects.

References:

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NR787 Wednesday, May 24, 3:00 PM - 5:00 PM

History of Childhood Abuse in Psychiatric Patients With and Without Drug Addiction

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the relationship between a history of abuse in childhood and different psychiatric disorders in the adult.

Summary:

Aims and objectives: To examine the relationship between history of childhood abuse and gender, diagnoses of schizophrenia and major depression, drug abuse, alcohol abuse, and suicide risk in patients admitted to a psychiatric brief hospitalization unit.

Methods: The sample included 241 psychiatric patients consecutively admitted to the psychiatric brief hospitalization unit of the Fundacion Jimenez Diaz general hospital in Madrid, Spain (2003-2004). Patients with mental retardation or dementia were excluded from the study. The assessment included a brief structured diagnostic interview (Mini International Neuropsychiatric Interview, MINI) to obtain DSM-IV psychiatric diagnoses. History of childhood abuse was recorded. The rates of childhood abuse were compared in male and female patients, in patients with and without major depression, schizophrenia, alcohol abuse and drug abuse, and in patients with different levels of suicide risk (no risk, mild, moderate and severe risk). Chi^2 tests were used for all the comparisons.

Results and conclusions: There were statistically significant differences between the rates of childhood abuse in patients with and without drug abuse (Fisher exact test p=0.09).There were no significant differences between the rates of childhood abuse in males and females (Fisher exact test p=0.36). There were no significant differences between the rates of childhood abuse in patients with and without alcohol abuse (Fisher exact test p=0.62), with and without schizophrenia (Fisher exact test p=0.57) and with and without major depression (Fisher exact test p=0.42). There were no significant differences among the rates of childhood abuse in patients with absent, mild, moderate and severe risk of suicide (Chi^2=3.03; df=3; p=0.39;).

References:

1. MacMillan HL, Fleming JE, Streiner DL et al.Chilhood abuse and lifetime psychopathology in a community sample. Am J Psychiatry 2001;158: 1879-83.
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NR788 Wednesday, May 24, 3:00 PM - 5:00 PM

Sociodemographic Characteristics of Substance Users Among Trauma Inpatients

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to:

1. Demonstrate knowledge of the prevalence of specific substance use and substance use disorders among severely injured trauma inpatients
2. Recognize the sociodemographic characteristics associated with specific substance use and substance use disorders among severely injured trauma inpatients

Summary:

Substance use is often associated with physical trauma. However, little is known regarding the prevalence of specific substance use disorders and the sociodemographic characteristics associated with substance use among severely injured patients. We evaluated these issues in an unselected sample of 1,118 adult inpatients at the Shock-Trauma Center, Baltimore, MD interviewed with the substance use disorders section of the Structured Clinical Interview for DSM-III-R. The association of subject sociodemographic characteristics with substance use status and comparisons of subjects with different substance use status were analyzed using multinomial logistic regression models. Most subjects (888, 79.4%) reported lifetime use of at least one substance: 382 (34.2%) only alcohol, 85 (7.6%) only illegal drugs, and 421 (37.7%) both alcohol and a drug. Rates of lifetime substance use, lifetime abuse/dependence, and current abuse/dependence for specific substances were alcohol-71.8%/43.6%/32.1%, marijuana-37%/18.2%/9.6%, cocaine-23.1%/17.8%/11.8%, opiates-18.2%/14%/9.9%, hallucinogens-6.2%/2.3%/0.6%, sedative-hynpotics-5.6%/1.7%/0.7%, other stimulants-4.6%/2%/0.6%. Lifetime alcohol users were significantly more likely than nonusers to be male (adjusted odds ratio [aOR] = 1.7); users of illegal drugs were also

more likely to be younger than 33 years (aOR = 1.8) and poor (annual income < $10,000) (aOR = 1.8) and less likely to be married (aOR = 0.5). Patients with current drug abuse/dependence were significantly less likely than other patients to be white (aOR = 0.4) and high school graduates (aOR = 0.5), and more likely to be poor (aOR = 2.9); those with current alcohol abuse/dependence were also more likely male (aOR = 2.2) and less likely married (aOR = 0.4) and younger (aOR = 0.4). These findings highlight the need for screening for substance use disorders in trauma settings.

Supported by NIH grant RO1-AA09050, the Intramural Research Program of the National Institutes of Health, National Institute on Drug Abuse, and a Brazilian National Council of Research postdoctoral scholarship to Dr. Martins.

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2. Gentilello LM, Rivara FP, Donovan DM, Jurkovich GJ, Daranciang E, Dunn CW, Villaveces A, Copass M, Ries RM: Alcohol interventions in a trauma center as a means of reducing the risk of injury recurrence. Ann Surg 1999; 230:473-483.

NR789 Wednesday, May 24, 3:00 PM - 5:00 PM

Cocaine Use Milestones in Male Cocaine Addicts

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to

1. Recognize common adverse consequences of cocaine use.
2. Identify risk factors for rapidly developing cocaine-related problems.

Summary:

One measure of the addiction liability of a substance is the rapidity with which users progress through various milestones, e.g., from first use to regular use, problematic use, and treatment. We used this approach in a convenience sample of 83 adult male cocaine addicts (mean [SD] age 34.8 [7.4] years, 7.3 [5.2] years of cocaine use) undergoing inpatient treatment who gave detailed retrospective self-report. Subjects first used cocaine at age 27.5 [9.0] years, first used regularly 3.4 [4.3] years later, had first cocaine-related problems 10.6 [7.7] months after that, and first entered treatment 30.9 [27.5] months thereafter. Subjects who first used cocaine by smoking (half of sample), rather than intranasally ("snorting"), had shorter intervals to first regular use (22.7 versus 57.1 months [p = 0.002]) and to first cocaine-related problems (34.1 versus 67.0 months [p =0.006]), and a trend towards shorter interval between first problems and treatment entry (25.7 versus 36.8 months [p = 0.07]). Subjects whose first regular use was by smoking (85% of sample) also had a shorter interval between first problems and treatment entry (27.5 versus 54.1 months [p = 0.04]). Age at first cocaine use was not associated with significant differences in intervals between milestones. The progression along these milestones was faster for these cocaine addicts than has been reported for patients with alcohol dependence, suggesting the high abuse liability of cocaine. The smoked route of administration was associated with faster progression, consistent with the putative greater abuse liability of this route over intranasal administration.

Supported by Novartis Pharmaceuticals Corp. and the Intramural Research Program of the National Institutes of Health, National Institute on Drug Abuse.

References:

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NR790 Wednesday, May 24, 3:00 PM - 5:00 PM

A Multicenter Investigation of the Opioid Antagonist Nalmefene in the Treatment of Pathological Gambling

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Educational Objectives:

At the conclusion of this presentation the participant should be able to understand that pharmacotherapy may be beneficial for pathological gambling and recognize the difficulties in treating individuals with pathological gambling.

Summary:

Objective: Pathological gambling (PG) is a disabling disorder experienced by approximately 1-2% of adults and for which there exist few empirically validated treatments. This study examined the efficacy and tolerability of the opioid antagonist nalmefene in adults with PG.

Method: A 16-week, randomized, dose-ranging, double-blind, placebo-controlled trial was conducted at 15 outpatient treatment centers across the United States between March 2002 and April 2003. 207 persons with DSM-IV PG were randomized to nalmefene (25mg/d, 50mg/d or 100mg/d) or placebo. Primary outcome, the Yale Brown Obsessive Compulsive Scale Modified for Pathological Gambling (PG-YBOCS), was statistically analyzed using a linear mixed-effects model.

Results: Using estimated regression coefficients, the 25mg/d and 50mg/d groups showed significant difference from placebo (p=.007 and p=.016, respectively) on the PG-YBOCS. 59.2% of subjects assigned to 25mg/d were "much improved" or "very much improved" at the last evaluation, compared to 34.0% of those taking placebo (odds ratio=2.79; 95% CI: 1.21-6.41; p=0.033). Adverse experiences included nausea, dizziness and insomnia.

Conclusions: Nalmefene demonstrated statistically significant reduction in PG severity. Low dose (25mg/d) appeared efficacious with few adverse events. Higher doses (50mg/d and 100mg/d) resulted in intolerable side effects.

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NR791 Wednesday, May 24, 3:00 PM - 5:00 PM

Psychodynamic Therapy for Co-Occurring Borderline Personality Disorder and Alcohol Use Disorders: A Newly Designed Ongoing Study

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Kang, M.D., Anna L. Remen, Ph.D., Maureen G. Soderberg, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to:

1. Understand the need to develop specific treatments for persons with co-occurring borderline personality disorder and alcohol use disorders.
2. Describe the research design of a study evaluating novel and specific treatment for this co-occurring subgroup.

Summary:

Objectives: The authors describe an on-going study evaluating the 12-month efficacy of a novel treatment, labeled dynamic deconstructive therapy (DDT), developed specifically for co-occurring BPD and alcohol use disorders (AUD). Co-occurrence is common and has been associated with a worsened course and prognosis of both disorders. DDT is time-limited, manual-based and involves individual sessions on a weekly basis.

Methods: 30 adults with co-occurring BPD/AUD were randomized into treatment as usual (TAU) or DDT. Exclusion criteria included age > 45 years, primary psychotic or neurological diagnosis, or mental retardation. Primary outcomes include parasuicides, alcohol misuse, and inpatient utilization assessed every 3 months over a 12-month period.

Preliminary Results: Recruitment ended 11/16/05. 103 potential participants were screened, 73 were excluded of whom 41 did not meet inclusion criteria, and 30 were randomized into TAU (n= 15) or DDT (n=15). Participants are mostly female (83%) and unemployed (62%) with a mean age of 28.7 +/- 7.7 years. DDT therapists include the P.I. (n=6 participants) and five psychiatry residents trained to competency (n=9 participants). Outcome data has been completed so far for n=17 participants at 3 months and n=13 at 6 months. Both groups are improving by > 50% on the primary outcome measures by 6 months with tendencies favoring DDT. Retention in psychotherapy has been 80% at 3 months for DDT, but only 14% for participants receiving TAU.

Conclusions: DDT is feasible to train and implement and may be associated with superior treatment retention in this highly impaired co-occurring subgroup.

References:

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2. Gregory RJ: The deconstructive experience. Am J Psychotherapy (in press).

NR792 Wednesday, May 24, 3:00 PM - 5:00 PM

Relationship Between Initial Trauma Reaction, ED Vital Signs, Drug and Alcohol Use in Acute Trauma Exposure

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to demonstrate knowledge of relationships between the presence of alcohol and drugs in addition to psycho-physiological responses in acutely traumatized individuals treated in an urban ED trauma center.

Summary:

Introduction: Peri-traumatic reaction and Emergency Department (ED) vitals signs have been shown to predict posttraumatic stress disorder (PTSD) in several studies. None have included alcohol and substance use, which is common among acute trauma victims. *Hypothesis*: The objective of this exploratory analysis was to evaluate whether there is a relationship between the presence of alcohol and substances in addition to psycho-physiological responses in acutely traumatized individuals treated in an urban ED trauma center. *Methods*: Subjects were recruited from Howard University ED. Based on the DSM-IV A1 trauma criteria, individuals were asked to complete several trauma-based self-reports and psychosocial measures. Vital signs and cardiac impedance were measured in ED patients who were evaluated following a life-threatening experience. *Results:* 22 of the 78 individuals preliminarily identified were consented and evaluated. Based on self-report assessments, individuals endorsed the use of alcohol and substances within 30 days prior to the traumatic incident. The prevalence of use was 77% for alcohol, 41 % for marijuana, and 23 % for cocaine. Subjects using cocaine had lower heart-rate during initial ED assessment yet endorsed greater somatic physical reaction whereas subjects with alcohol use reported lower peri-traumatic distress. *Conclusion*: The data suggests that the use of alcohol and substances prior to traumatic incidents has complex influences on peri-traumatic responses and ED vital signs.

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NR793 Wednesday, May 24, 3:00 PM - 5:00 PM

Patterns of Antipsychotic Utilization Among Patients With Schizophrenia in a State Medicaid Program

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Educational Objectives:

At the end of this presentation, the participant should: 1) be aware of the various patterns of antipsychotic utilization and high rates of non-adherence to antipsychotic therapy among patients with schizophrenia; and 2) recognize the factors that are associated with different types of antipsychotic utilization patterns.

Summary:

Summary:

Objectives: To evaluate antipsychotic utilization patterns such as polytherapy, switching, non-adherence and adherence, and to identify predictors of these utilization patterns.

Methods: Data for patients with schizophrenia with at least two antipsychotic prescriptions filled between January 1, 1999 and December 31, 2001 were extracted from a 'de-identified' Medicaid database. Patients with major depression were identified according to ICD-9-CM. Patients were classified into pre-specified treatment cohorts (polytherapy, switching, non-adherent, and adherent) based on antipsychotic prescription refills during a 12-month follow-up period. Adherence was defined as patients receiving ≥80% of the total days' supply of antipsychotics during the follow-up period. Multinomial logistic regression was used to test

whether factors such as patient characteristics, antipsychotic type, and prior healthcare utilization were associated with antipsychotic utilization patterns.

Results: Patients were classified into polytherapy (N=124, 12.0%), switching (N=132, 12.7%), non-adherent (N=588, 56.8%), and adherent (N=192, 18.5%) cohorts. Alcohol and substance abuse and typical antipsychotic use were significantly associated with polytherapy, switching, and non-adherence (odds ratios of these associations ranged from 1.1 to 5.5, $P<0.01$). Patients with major depression (N=178) were more likely to have polytherapy than adhere to antipsychotic therapy (OR=2.3, $P<0.01$). Mood stabilizer and antidepressant use were associated with non-adherence (OR=0.7, $P<0.01$) and switching (OR=1.3, $P<0.01$), respectively.

Conclusion: Non-adherence rates were high among patients with schizophrenia receiving antipsychotics. Typical antipsychotic use and alcohol and substance abuse were associated with polytherapy, switching, and non-adherence.

Funding for this research was provided by AstraZeneca Pharmaceuticals LP

References:

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2. McCombs, J.S., Nichol, M.B., Stimmel, G.L., Shi, J., Smith, R.R. (1999) Use patterns for antipsychotic medications in medicaid patients with schizophrenia. J Clin Psychiatry 60(Suppl 19):5-11.

NR794 Wednesday, May 24, 3:00 PM - 5:00 PM

Impact of Antipsychotic Use on Mental Health-Related Hospitalizations Among Patients With Schizophrenia in a State Medicaid Program

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Educational Objectives:

At the end of this presentation, the participant should be able to compare differences in psychiatric hospitalizations among patients with schizophrenia initiated on different antipsychotics.

Summary:

Summary:

Objectives: To compare psychiatric hospitalization rates, length of stay, and costs among patients with schizophrenia initiated on antipsychotics in a state Medicaid system. **Methods:** Retrospective claims study of patients with schizophrenia from a 'de-identified' Medicaid database. Patients were assigned to quetiapine (QTP), olanzapine (OLZ), risperidone (RIS), or typical antipsychotic treatment groups based on the first prescription filled between January 1, 1999 and December 31, 2001. Hospitalizations in the 12 months before and after antipsychotic initiation were analyzed. **Results:** Hospitalization rates decreased (6-8%) in the atypical antipsychotic cohorts and increased (2.6%) in the typical antipsychotic cohort. Logistic regression revealed no significant difference in hospitalization risk between antipsychotic cohorts. Length of stay (days) and costs were similar among atypical antipsychotic cohorts (QTP=9.9±12.6 and $4,865±$11,285; OLZ=12.6±13.6 and $4,813±$11,309; RIS=10.2±9.4 and $4,247±$11,285), but the typical antipsychotic cohort had a longer length of stay and higher costs (13.4±11.0 and $5,418±$15,787). Multiple regression revealed significantly higher costs (3.7%, $P<0.05$) for the typical antipsychotic cohort compared with the QTP cohort. **Conclusions:** There were no significant differences in hospitalization risk between antipsychotics. Length of stay and costs were similar between atypical antipsychotics, although the QTP cohort demonstrated lower costs compared with the typical antipsychotic cohort.

Funding for this research was provided by AstraZeneca Pharmaceuticals LP

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NR795 Wednesday, May 24, 3:00 PM - 5:00 PM

Mothers With Thoughts of Murder: Psychiatric Patterns of Inquiry

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Educational Objectives:

Objectives: At the end of this presentation, the participant should be able to: (1) recognize the rates of filicidal thoughts among depressed mothers with young children, and (2) be more comfortable routinely inquiring about filicidal thoughts among psychotic, depressed, or suicidal mothers.

Summary:

Child murder by mothers is an important public health concern, and in some cases is linked to maternal mental illness. However, based on clinical and forensic experience, it appeared that psychiatrists did not routinely inquire of their female patients whether they have thoughts of harming their children. In this survey (N= 194), psychiatrists were asked about whether they routinely query women about motherhood and about these thoughts. Our results indicated that the majority of psychiatrists believe that they inquire about motherhood in their female patients a great majority (90-100%) of the time. While many psychiatrists reported that they inquire about filicidal thoughts among both psychotic mothers and suicidal mothers, many only ask about homicidal thoughts in general. Often psychiatrists would be willing to discuss filicide cases that have been in the news with their patients. The majority of psychiatrists also underestimated the percentage of depressed mothers of young children with filicidal thoughts. Suggestions for further education of psychiatrists, and for increased comfort in inquiring about filicidal thoughts will be made.

References:

1. Friedman SH, Horwitz SM, Resnick PJ: Child murder by mothers: a critical analysis of the current state of knowledge and a research agenda. Am J Psychiatry 2005;162(9):1578-87.
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NR796 Wednesday, May 24, 3:00 PM - 5:00 PM

Pharmacogenetic Modulators of Fetal Exposure to Medicine

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Educational Objectives:

At the conclusion of this session, the participant should be Able to: understand the relationship between the C3435T SNP and relative fetal drug exposure.

Summary:

To date, we know all psychotropic medications taken during pregnancy reach the fetus. However, multiple factors, ex. drug transporters, that govern not only fetal exposure but neonatal clearance are not well studied. Metabolic capacity of the infant is determined by mom and dad, while, metabolic capacity of the placenta is determined by mom, dad, and baby. Poor metabolizer genotypes should be a significant factor in fetal drug exposure by increasing maternal plasma drug concentration, which would result in increased drug transfer to the fetus via umbilical vein. The potential P-glycoprotein (P-gp) factors that affect fetal exposure are the alleles of C3435T (homozygous versus heterozygous). Interpreting the data to predict fetal exposure requires consideration that the varying genotype combination of the mother and the placenta may be important in influencing the rate and extent of fetal exposure and clearance. We have enrolled 65 women at the Women's Mental Health Program on various medicines. We collected maternal and infant DNA. In the preliminary data we focused on the P-gp (maternal and infant pairings) of women taking sertraline (n=15) during pregnancy to assess which polymorphism of C3435T may influence drug exposure. Maternal and infant pairs with the homozygous C alleles had a mean plasma ratio of 0.350+ 0.059ng/ml. Maternal and infant pairs with a homozygous T alleles had a mean plasma ratio 1.050ng/ml. The T alleles for C3435T are associated with reduced P-gp activity leading to higher plasma concentrations of its substrates. Understanding the role of P-gp in moderating transplacental passage of substrates has important clinical implication for choosing medications to minimize fetal drug exposure while achieving therapeutic objectives for the patient during pregnancy.

Supported by P50-MH-68036

References:

1. DeVane, CL. Pharmacogenetics and Drug Metabolism of Newer Antidepressant Agents 1994.
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NR797 Wednesday, May 24, 3:00 PM - 5:00 PM

Substance Abuse Disorders as Risk Factors for Psychiatric Hospitalization in 2,963 Patients With Bipolar Disorder

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Educational Objectives:

At the conclusion of this presentation the participant should be able to identify those patient with bipolar disorder who are at high risk for admission to psychiatry.

Summary:

Objective: To develop profiles of risk factors for psychiatric hospitalization in a large sample of veterans with bipolar disorder so healthcare needs may be planned and interventions targeted.

Method: This retrospective study used the administrative database maintained by the Veteran's Affairs Health Care System, Palo Alto, fiscal year 2003-2004 to extract data for patients who had been diagnosed with bipolar disorder (Types I, II, and NOS). Predictors used included age, gender, ethnicity, and presence of comorbid substance use disorders. A Receiver Operator Characteristic (ROC) was used to determine the association of the predictors with inpatient hospitalization.

Results: The 2,963 patients with bipolar disorder had an overall risk of psychiatric hospitalization of 20%. Veterans with bipolar disorder and alcohol use disorder had a 43% risk of hospitalization. Those with an additional diagnosis of polysubstance dependence (PSD) had a risk of 57%. Subjects with alcohol use disorders and PSD who were also separated from their spouse/partner were all admitted (100%).

Patients with bipolar disorder who did not have an alcohol use disorder, but who were separated from their spouse/partner, had a risk of hospitalization of 76%. Within this group, those with a diagnosis of PSD had a risk of 37%. Increased risk of hospitalization was also found with cannabis dependence (risk of 33%), cocaine dependence (risk of 38%), amphetamine dependence (risk of 32%) and opiate dependence (risk of 39%). Furthur analysis revaled that age greater than 52 years predicted a longer inpatient stay (>14 days).

Conclusions: High rates of alcohol and substance use are reported in bipolar patients

(Cassidy, 2001) and annual societal costs of bipolar disorder approach $45 billion (Sajatovic, 2005). Comorbid alcohol use, polysubstance dependence, and marital separation increased the risk of psychiatric hospitalization in this population.

References:

1. Cassidy F, Ahern EP, Carroll BJ. Substance abuse in bipolar disorder. Bipolar Disorders 2001; 3: 181-188.
2. Sajatovic M. Bipolar Disorder: Disease Burden. Am J Manag Care 2005; 11:3 Suppl. 80-84.

NR798 Wednesday, May 24, 3:00 PM - 5:00 PM

The Associated Factors of Low Bone Density Among Depressive Women

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Educational Objectives:

low bone density in depressive women and associated factors

Summary:

Previous studies suggested that depression might be associated with low bone mineral density (BMD) in depressive women. We conducted a prospective cross- sectional study explored the associated factors of bone density among 121 major depressive women diagnosed by MINI structured interview. And all had been ruled out any endocrine and biochemistry abnormalities, including thyroid/ parathyroid function, anemia, and Vit12 deficiency and so on. The total 100 depressive 100 women received self-rated Beck Depression Inventory (BDI) and HAMD-17 rating scale. BMD of total body was measured by dual X-ray densitometry (DEXA) using the Hologic Delphi QDR-2000 densitometry.

The mean age is 48.3 $\pm$ 10.2 years, and BMI is 24.2 $\pm$ 4.2. The mean BMD is -1.14 $\pm$ 0.96 (-3.90 to 0.90 g/cm^2), and reach the criteria of osteopenia (T-score <=-1.0). We found age, family history of osteoporosis, high BMI, consumptions of coffee or tea, and depression severity are associated with low BMD. Depression severity, consumption of tea and coffee, family history of osteoporosis and age accounted for 28 % variance of bone density by logistic regression.

These results suggest depression is associated with lower BMD and the above-mentioned associated factors should be more educated in depressive women. The normal control group (100 nor-

mal, non-depressive health women) is under evaluation till now. Then we could compare the possible interesting differences between the two groups in the near futhre.

References:

1. Jacka FN: Depression and bone mineral density in a community sample of perimenopausal women: Geelong Osteoporosis Study.Menopause 2005; 12:88-91.
2. Konstantynowicz J: Depression in anorexia nervosa: a risk factor for osteoporosis. J of Clin Endocrinology & Metabolidm 2005; 90:5382-5385.

NR799 Wednesday, May 24, 3:00 PM - 5:00 PM

The Effect of Smoking Cessation on the PANSS in Chronic Schizophrenic Patients

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to the effect from smoking cessation on the symptomatology observed in patients with schizophrenia.

Summary:

Background: Smoking has been identified as a severe public issue worldwide since last century. More schizophrenic patients stayed on smoking compared to the general population, which indicates more quit-smoking should be practiced in this minor group. Past publications showed equivocal points on the effects of smoking on psychotic symptoms among these schizophrenic patients. This study tries to reveal the phenomenon observed in Taiwan samples. **Methods:** This is a 3 year, investigator-initiated study project. Here we planed to enroll 500 inpatients meeting DSM-IV criteria for schizophrenia or schizoaffective disorder from a Taiwan based psychiatric hospital during the study. Patients were taking a variety of conventional and atypical antipsychotic medications with a confident compliance. All subjects after consent form completed were evaluated for clinical symptoms immediately by using PANNS scale at baseline and 4 weeks after Nicotine Patch Replacement Therapy Initiation. **Results:** After adjusted for age and hospitalization days, the change of PANNS scale between baseline and 4 weeks later did not reach to a significant level at all, no matter categorized into positive, negative, or general subdivision of the scale. **Conclusions:** This study might give some clues in the debate between benefits or damages from smoking itself on the symptomatology from the view of Taiwan.

References:

1. Aguilar MC, Gurpegui M, Diaz FJ, de Leon J. Nicotine dependence and symptoms in schizophrenia: naturalistic study of complex interactions. Br J Psychiatry. 2005;186:215-21.
2. Strand JE, Nyback H. Tobacco use in schizophrenia: a study of cotinine concentrations in the saliva of patients and controls. Eur Psychiatry. 2005;20(1):50-4.

NR800 Wednesday, May 24, 3:00 PM - 5:00 PM

New Research of Sleep and Dream in Schizophrenia

Nikola Ilankovic, Prof. Dr. *Institute of Psychiatry, Neuropsychiatry, Pasterova 2, Belgrade, YU-11000, Serbia and Montenegro*, Andrej Ilankovic, M.D., Tanja Lakovic, M.D., Vera Ilankovic, Prof. Dr., Lana Marija Ilankovic

Educational Objectives:

After this session the participants will get new knowledge about neurophysiological models of sleep disturbances in acute and chronic schizophrenic states.

Summary:

Aims: Polysomnographic (PSG) measurement of sleep by schizophrenic patients to investigate models of sleep disturbances in schizophrenia.

Methods:

Neurophysiological measurement of sleep using electroencephalography (EEG), electrooculography (EOG) and electromyography (EMG) was carried out in 30 patients with an acute schizophrenic state (F 23.1 & F 23.2 in ICD-10) and in 30 patients with a chronic/residual schizophrenic state (F 20.5 in ICD-10). Recording of sleep patterns (according to Rechtschaffen & Kales), statistical analysis and estimation of the discriminative models of sleep was made in these two groups of psychotic patients. The Electrophysiological Profile of Sleep (EPS) was derived from these measures and contained 130 variables of nocturnal sleep. Statistical analysis was by step-wise discriminative function analysis.

Results:

The most discriminative variable in this battery was the Index of Endogenous Periodicity/Perturbation (IEP-P1): IEP-P1=REM-1/NREM-1, where REM-1 and NREM-1 are the first periods of REM and NREM sleep, respectively. Two patterns were seen:

1. The Index of Endogenous Perturbation (IEP-P1) was *LOW* in the first group which we call the *"REM DEFICIT"* type of sleep disturbance (with reduction of "REM-1 phase ") in acute schizophrenic states; IEP-P1 < 0.3.
2. The IEP-P1 index was *HIGH* in the second group which we call the *"DELTA DEFICIT"* type of disturbed sleep (with reduction of "delta-sleep ") in chronic schizophrenia states; IEP-P1 > 2.40.

Conclusions:

1. The results of our investigations demonstrate that the Index of endogenous sleep perturbation (IEP-P1) is a highly reliable indicator of sleep disturbance in acute and chronic schizophrenic states.
2. This sleep index is very low in acute and very high in chronic/residual schizophrenia states.
3. We propose the IEP-P1 as a possible state marker in schizophrenia.

References:

1. Ilankovic N., Ilankovic A.Sleep and Dreams, Belgrade, 1999.
2. Sadock: Synopsis of Psychiatry, LWW, 2004.

NR801 Wednesday, May 24, 3:00 PM - 5:00 PM

ADHD: New Treatment With the Vilan Method®

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Educational Objectives:

The participants can learn the functional psychomotoric assessment of ADHD and the application of neurorehabiliation method VILAN.

Summary:

Objective: Evaluation of effects of neurorehabilitation of hyperkinetic psychomotor disturbaces with with VILAN method by children with ADHD. Method: In clinical study of 30 children (mean age 7.4 years) with ADHD. All participants met DSM-IV criteria for ADHD.

The assessment of ADHD was with: ADHD Rating Scale and with VILAN functional psychomotor assesment. The assessment of other psychomotor disturbances was with clinical rating scales for: Abnormally Involuntary Movement Scale (AIMS, Gay), Depressive (psychomotor) Retardation Scale (DRS, Widlocher), Praxia Scale (Brown). L-R Orientation Test and Simultaneous Movement Test (TSM, V. Ilankovic, 1995). In treatment with VILAN method we divided the patients in 2 subgroup: in 1. group the treatment ADHD was with "ADHD Drugs" + VILAN rehabilitation method, and in 2. group only with VILAN method. The first assessment of effects of treatment was after 4 weeks. Results: Our results were in **1. group**: reduction of - ADHD symptoms for 45 %, dyspraxio for 86 %, disorders of simultan movements for 64 %, depressive retardation for 48 %, speech for 32% and abnormal movements for 24 %. In **2. group**: reduction of - ADHD symptoms for 35 %, dyspraxio for 90%, disorders of simultan movements 78% ($p<0.01$), depressive retardation for 72% ($p<0.001$), speech 48% ($p<0.01$) and abnormal movements for 46% ($p<0.001$). Conclusions: 1.The most of children with ADHD have a serious psychomotor disturbances, too (multiple handicaps). 2. Many of children have chronic infecitive diesease, which need a specific therapy, too! 3. Applying of early motor rehabilitation (VILAN method) in integrative treatment is obligatory for functional recovery, normal development and quality of life. 4. The pharmacotherapy with ADHD drugs can result with higher improvement of psychomotor dysfunctions. 5. The early continuous psychomotor rehabilitation with VILAN Method by ADHD is a good chance to prevent (diminish) the late psychomotoric deficits by this patients.

References:

1. Ilankovic N., Ilankovic V. Restaurative psychiatry. Belgrade, Medical faculty, 1999.
2. Ilankovic V., Ilankovic N. Vilan Method, Belgrade. Medical faculty, 1997.

NR802 Wednesday, May 24, 3:00 PM - 5:00 PM

Body Weight and Serum Lipid Levels in Young Women Treated With Valproate Versus Lamotrigine

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the differential effects of one year of treatment with valproate versus lamotrigine on body weight and serum lipid levels in young women with epilepsy.

Summary:

Objective: To evaluate the impact of valproate (Divalproex®, VPA) or lamotrigine (LAMICTAL®, LTG) on body weight and serum lipid levels in women with epilepsy(WWE).

Background: Weight gain and untoward changes in serum lipid levels have been reported in women taking VPA for epilepsy, whereas LTG does not appear to affect body weight or serum lipid levels.

Methods: Eligibility criteria for this multicenter, prospective, randomized, open-label study(LAM30007) included age 13-40 years; regular menstrual cycles; no concurrent hormonal medications; no prior LTG or VPA; and either newly diagnosed or inadequately controlled epilepsy. Subjects were randomized to LTG or VPA and were treated for one year. Fasting serum lipid levels and body weight were measured at baseline and every three months. To exclude the confounding effect of puberty on the results, a post-hoc analysis was conducted in women who were more than two years post menarche. An ANCOVA model comparing end of study measurements to baseline was used, with baseline measures and study center as covariates.

Results: A total of 363 women (177 LTG, 186 VPA) were evaluated. Mean weight gain in the VPA group was 2.8 kg (SD=3.35) and 0.2 kg (SD=3.9) in the LTG group, $p<0.001$. Mean serum triglycerides increased 8.4 mg/dL (SD=37.5) in women taking VPA, while they decreased slightly in the LTG group, 0.2 mg/dL (SD=36.3), $p=0.019$. The serum total cholesterol levels showed a slight decrease in both treatment groups, but there was a mean decrease of 2.6 mg/dL (SD=10.3) in HDL cholesterol in VPA treated women, while a slight increase of 0.6 mg/dL (SD=9.2) was observed in the LTG group, $p=0.001$.

Conclusion: This large, multiethnic, prospective, randomized study indicates that VPA is associated with weight gain and unfavorable changes in serum lipid levels in WWE, whereas LTG does not seem to affect body weight or serum lipid levels.

References:

1. Bilo L, Meo R, Nappi C, et al. Reproductive endocrine disorders in women with primary generalized epilepsy. Epilepsia 1988;29:612-9.
2. Isojärvi JIT, Tauboll E, Pakarinen AJ, et al. Altered ovarian function and cardiovascular risk factors in valproate treated women. Am J Med 2001;111:290-6.

NR803 Wednesday, May 24, 3:00 PM - 5:00 PM

HLA-DQB1 0602 and Hypocretin in Korean Narcoleptics With Cataplexy

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize High frequency of HLA-DQB1*0602 and low hypocretin level in cataplexy-positive groups suggest that cataplexy-positive narcoleptics may be a etiologically different disease entity from cataplexy-negatives.

Summary:

Objectives:

Cataplexy is one of the most pathognomonic symptoms in narcolepsy. This study was designed to investigate the clinical features, frequency of DQB1*0602 and CSF hypocretin levels in Korean narcoleptics with cataplexy to compare with those who have not cataplexy.

Methods:

72 narcoleptic patients were selected by nocturnal polysomnography and multiple sleep latency test(MSLT) as well as their history and clinical symptoms at Sleep Disorders Clinic of St. Vincent's Hospital, the Catholic University of Korea. The patients were divided into 56 cataplexy-positive narcolepsy group and 12 cataplexy-negative group. All patients were subjected to HLA typing for the presence of DQB1*0602 and spinal tapping for measuring the level of CSF hypocretin.

Results:

1. Mean positivity of HLA-DQB1*0602 of all narcoleptic patients were 83.3%(60 subjects). In cataplexy-positive patients, compared with cataplexy-negative patients, the positivity of HLA-DQB1*0602 was found to be significantly increased(51 subjects, 91.9% versus 9 subjects, 56.3%)($P=0.003$).

2. In 48 out of 56 cataplexy-positive patients(85.7%), hypocretin levels were decreased(≤110 pg/ml) or below the detection limit of assay(<40 pg/ml). However, onlt 6 out of 16 cataplexy-negative patients(37.5%) exhibited decreased hyopcretin level. And the

difference between two groups was statistically significant(P= 0.000).

3. Cataplexy-positive group(mean age; 25.3 ± 10.4, 34 men and 22 women), compared with cataplexy-negative group(mean age; 29.8 ± 14.8, 13 men and 3 women), showed more frequent hypnagogic hallucinations(36 subjects, 64.3% versus 4 subjects, 25.0%)(P=0.005).

4. In nocturnal polysomnography and MSLT findings, there were no significant differences in all sleep parameters between cataplexy-positive and cataplexy-negative groups.

Conclusions:

High frequency of HLA-DQB1*0602 and low hypocretin level in cataplexy-positive groups suggest that cataplexy-positive narcoleptics may be a etiologically different disease entity from cataplexy-negatives. Additionally, Current criteria prevail for the diagnosis of narcolepsy need to be reclassified according to the presence of cataplexy or not.

References:

1. Mignot E, Hayduk R, Grumet FC, Black J, Guilleminault C: HLA DQB1*0602 is associated with cataplexy in 509 narcoleptic patients. Sleep 1997;20:1012-1020.
2. Lin L, Faraco J, Li R, Kadotani H, Rogers W, Lin X, Qiu X, Jong PJ, Nishino S, Mignot E: The sleep disorder canine narcolepsy is caused by a mutation in the hypocretin(Orexin) receptor 2 gene. Cell 1999;98:365-376.

NR804 Wednesday, May 24, 3:00 PM - 5:00 PM

Treatment of Mood and Hot Flushes With Duloxetine in Postmenopausal Depressed Women

Hadine Joffe, M.D. *Massachusetts General Hospital, Psychiatry, 185 Cambridge Street, Suite 2200, Boston, MA, 02114*, Claudio N. Soares, M.D., Brittny Somley, B.S., Laura Petrillo, M.D., Adele C. Viguera, M.D., Ruta M. Nonacs, M.D., Lee S. Cohen, M.D.

Educational Objectives:

Objectives:

1.To understand that the specific role of the SNRI duloxetine in treating depression in postmenopausal women.

2.To investigate if duloxetine also treats hot flushes in postmenopausal women with depression.

Summary:

Objective: Duloxetine (Cymbalta®) is a new SNRI that is effective in treating depression. However, its antidepressant effect has not been studied in postmenopausal women with hot flushes. Evidence also suggests that other SSRI/SNRI reduce hot flushes in women with and without depression. We examined whether duloxetine treats depression and hot flushes in postmenopausal women with depression.

Design: Postmenopausal women with major depression and hot flushes were enrolled in an 8-week open-label clinical trial. At study-entry, all subjects were off hormonal therapy and had MINI-rated major depression, a Montgomery-Åsberg Depression Rating Scale (MADRS) score >20, and significant menopausal symptoms (Greene Climacteric Scale [GCS] total score >20, GCS vasomotor subscale score >3, or >14 hot flushes/week). After a 2-week single-blind placebo run-in, all subjects not responding to placebo were treated for 8 weeks with flexible dosing of duloxetine 60-to-120-mg/day. Changes in mood and hot flushes were assessed using the MADRS and GCS, respectively. This presentation represents an interim analysis, with all subjects expected to complete over the next few months.

Results: To date, 17 women have enrolled in the study and 9 (mean age 52) have been eligible for treatment after the placebo run-in. MADRS scores improved significantly from 24.5 + 2.8 to 5.0 + 4.1 (p<0.001) with duloxetine therapy (final dose 81.4 + 22.7 mg/day). Menopausal symptoms improved significantly, with GCS total and vasomotor subscale scores decreasing from 24.8 + 4.4 to 9.2 + 3.4 (p=0.001) and 4.7 + 1.5 to 2.2 + 0.98 (p=0.004), respectively.

Conclusion: This interim analysis of an open-label clinical trial suggests that duloxetine treats depression as well as hot flushes in postmenopausal women who have both major depression and hot flushes. The beneficial effects noted for depression and hot flushes suggest that duloxetine may be a particularly useful agent in the treatment of symptomatic postmenopausal women.

References:

1. Joffe H, et al.: Assessment and treatment of hot flushes and menopausal mood disturbance. Psychiatr Clin North Am 2003 Sep;26(3):563-80.
2. Soares CN, et al.: Efficacy of citalopram as a monotherapy or as an adjunctive treatment to estrogen therapy for perimenopausal and postmenopausal women with depression and vasomotor symptoms. J Clin Psychiatry. 2003 Apr;64(4):473-9.

NR805 Wednesday, May 24, 3:00 PM - 5:00 PM

Randomized, Placebo-Controlled Trial of Quetiapine for the Treatment of Alcohol Dependence

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Educational Objectives:

At the conclusion of this session, participants should be able to evaluate the efficacy and tolerability of quetiapine relative to placebo in the treatment of alcohol dependence.

Summary:

Background: Atypical antipsychotics may be a useful treatment for alcohol dependence. Trial data has shown that clozapine reduces alcohol consumption among schizophrenic patients, and olanzapine reduces alcohol craving in alcoholics.[1,2] Quetiapine is a psychotropic agent structurally related to clozapine but with a favorable side effect profile, and therefore may be a promising medication for the treatment of alcohol dependence.

Methods: Male and female alcoholics (n=61, age 25-64 years) were included in a 12- week placebo-controlled trial. After detoxification, patients were randomized to receive quetiapine (n=29), escalated over 9 days up to 400 mg daily at bedtime, or placebo (n=32), with weekly brief counseling. The primary outcome measure was alcohol consumption measured by the Timeline Follow-back.

Results: Forty-seven subjects (77%) completed the trial, with no significant between-group difference in treatment retention (23/29 [79%] for the quetiapine group, and 24/32 [75%] for the placebo group; χ^2=0.160, ns). Quetiapine-treated patients (mean dose 303 mg) had a significantly lower prevalence of alcohol use (group by time interaction: Z=2.21, *P*=0.03) and a significantly lower prevalence of heavy drinking, defined as >3 standard drinks a day for women and >4 standard drinks per day for men (Z=2.57, *P*=0.01), compared to placebo-treated patients. Nine quetiapine-treated patients (31%) maintained complete abstinence compared to two placebo-treated patients (6%) (χ^2=6.3, *P*=0.012). Quetiapine was well tolerated and there were no medication-associated serious adverse events.

Conclusions: This study shows promising results for quetiapine in the treatment of alcohol dependence. Similar studies under more controlled conditions would help validate these findings.

Supported by funding from AstraZeneca Pharmaceuticals LP.

References:

1. Drake RE, Xie H, McHugo GJ, Green AI. The effects of clozapine on alcohol and drug use disorders among patients with schizophrenia. Schizophr Bull 2000;26(2):441-9.
2. Hutchison KE, Swift R, Rohsenow DJ, Monti PM, Davidson D, Almeida A. Olanzapine reduces urge to drink after drinking cues and a priming dose of alcohol. Psychopharmacology (Berl) 2001;155(1):27-34.

NR806 WITHDRAWN

NR807 Wednesday, May 24, 3:00 PM - 5:00 PM

Effect of Multiple Oral Doses of Escitalopram on the Systemic Availability of Ramelteon, an MT_1/MT_2 Receptor Agonist

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Educational Objectives:

At the conclusion of this session, the participant should be able to discuss the effects of escitalopram administration on the systemic exposure of ramelteon, a novel selective melatonin MT_1/MT_2 receptor agonist recently approved for the treatment of insomnia.

Summary:

Objective: To evaluate the potential effect of escitalopram on pharmacokinetics of the chronohypnotic ramelteon, a novel MT_1/MT_2 receptor agonist, and vice versa.

Methods: In this open-label study, 48 healthy adults received single dose ramelteon 8mg (n=24) or escitalopram 10mg (n=24) on Day 1. Following a 6-day washout, subjects received the alternate treatment once daily for 6 days. On Day 14, all subjects received both escitalopram 10mg and ramelteon 8mg. Blood samples were collected post-dose on Days 1 and 14. Least-squares means were calculated for comparison of pharmacokinetic parameters.

Results: Compared to ramelteon alone, coadministration with escitalopram increased systemic exposure of ramelteon (AUC_{0-inf}: 2.03 versus 2.58 ng•hr /mL; 90% CI: 102.6%, 156.7%; C_{max}: 1.54 versus 2.08 ng/mL; 90% CI: 101.2%, 180.3%). Escitalopram had no effect on systemic exposure of ramelteon's metabolite, M-II. Compared to escitalopram alone, coadministration with ramelteon had no effect on systemic exposure of escitalopram (AUC_{0-inf}: 288.5 versus 298.5 ng•hr/mL; 90% CI: 93.7%, 114.2%; C_{max}: 10.37 versus 9.53 ng/mL; 90% CI: 76.5%, 110.5%) or its active metabolite, desmethylcitalopram. Adverse events occurred in 24 subjects during escitalopram administration, 16 subjects during ramelteon administration, and 15 subjects during coadministration; most adverse events were considered mild.

Conclusion: The presence of escitalopram increased ramelteon total exposure by 27% and C_{max} by 35%; however, this was not considered clinically relevant due to ramelteon's highly variable inter-subject pharmacokinetic profile (CV for AUC>100%) and its wide safety margin. Ramelteon had no effect on the availability of escitalopram. These results suggest that no dosage adjustments will be required when these drugs are taken together.

References:

1. Karim A, Tolbert D, Cao C: Disposition kinetics and tolerance of escalating single doses of ramelteon, a high affinity MT1 and MT2 melatonin receptor agonist indicated for treatment of insomnia. Journal of Clinical Pharmacology. In press.
2. Zammit G, Roth T, Erman M, Sainati S, Weigand S, Zhang J: Double-blind, placebo-controlled polysomnography and outpatient trial to evaluate the efficacy and safety of ramelteon in adult patients with chronic insomnia. Sleep 2005;28:A229.

NR808 Wednesday, May 24, 3:00 PM - 5:00 PM

Comparison of A.A.'s 12 Steps with Buddhism's Fourfold Noble Truth and Noble Eightfold Path

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize as follows. First, Alcoholics Anonymous(A.A.)'s Twelve Steps and Buddhism's Fourfold Noble Truth and Noble Eightfold Path are similar. Second, on the basis of the similarity, A.A.'s Twelve Steps originating in the Western Christianity could be practiced in the Oriental countries like Korea.

Summary:

Objective: Alcoholics Anonymous(A.A.) is effective in alcohol dependence treatment. A.A.'s twelve steps originating in the Western Christianity are practiced in Korea with Oriental tradition. We studied to find out a religious reason for the applicability of the 12 steps in Korea.

Method: The 12 steps were compared with Buddhism's Fourfold Noble Truth and Noble Eightfold Path.

Results: The 12 steps and the Buddha's teachings can be compared as follows. In terms of the Fourfold Noble Truth, the Truth of the Cause of Suffering can be matched with the first half of Step One; the Truth of Suffering, the second half of Step One; the Truth of the Cessation of Suffering, Step Two; and the Truth of the Noble Path to the Cessation of the Cause of Suffering, Step Three. For the Noble Eightfold Path, Right View can be paired with Step One-Three; Right Thought, Step Four-Five; Right Speech, Step Six-Seven; Right Behavior and Right Livelihood, Step Eight-Nine; Right Effort, Step Ten; Right Mindfulness, Step Eleven; and Right Concentration, Step Twelve.

Conclusions: These similarities might make the 12 steps acceptable to Korea, an Oriental country.

References:

1. Jeon JS: What the Buddha Taught and Noble Eightfold Path. Seoul, Korea Pali Text Society, 2002.
2. Bukkyo Dendo Kyokai: The Teaching of Buddha. Tokyo, Buddhist Promoting Foundation, 1975.

NR809 Wednesday, May 24, 3:00 PM - 5:00 PM

Psychiatric Symptoms and Neurocognitive Functions in Relation to Brain MRI Findings in the Traumatic Brain Injury Patients

Soo In Kim, M.D. *Ewha Womans University, PSYCHIATRY, Ewha Womans University Dong Dae Mun Hospital, 70, Chongro 6-ka, Chongro-ku, SEOUL, 110-783, Republic of Korea*, Jimin Kim, M.D., Yumi Sung, M.D., Weonjeong Lim, M.D., Kyu Wol Yun, M.D., Young-Chul Kim, M.D.

Educational Objectives:

Usually we supposed that neuropsychiatric sequelae after the traumatic brain injury is proportionated with the severity of trauma. Brain imaging is one of the measure reflect the severity of trauma. Our purpose was to compare psychiatric symptoms and neurocognitive functions between normal MRI finding group and abnormal MRI finding group after TBI. In addition, we investigated whether

the severity of trauma would correlate with the patients' subjective symptoms.

Summary:

Objective: The relationship between neuropsychiatric sequelae and MRI(MRI) findings in the traumatic brain injury(TBI) patients is still debated. This study has compared psychiatric symptoms and neurocognitive functions between normal MRI finding group and abnormal MRI finding group after TBI. In addition, we investigated whether the severity of trauma would correlate with the patients' subjective symptoms.

Method: 39 patients (34 males, 5 females) who have experienced mild to moderate closed head trauma have been assessed using Hamilton rating scale for depression(HAMD), Hamilton anxiety scale(HAMA), Functional assessment scale(FAS) and potential indicator of malingering(PIM) by two psychiatrists. All patients also have completed Symptom check list(SCL-90-R), Beck depression inventory(BDI), State-trait anxiety inventory(STAI), and Korean version of the SmithKline Beecham 'Quality of Life' scale(KvSKQOL). In addition, Korean Wechsler Adult intelligence Scale (K-WAIS), Rey-Kim Memory Scale(R-KMS), and Kims Frontal-executive neuropsychological test(KF-ENT) were assessed.

Results: Abnormal MRI finding group has shown significantly higher scores of FAS($p<0.05$). Other subjective or objective psychiatric symptoms and cognitive functions were not significantly different between two groups. The severity of the trauma was significantly correlated with the FAS scores($r=.46$, $p<.01$).

Conclusion: This study suggests that regardless of the severity of the trauma or persisting abnormal brain lesion, most of the patients have subjective and objective neuropsychiatric complications after head trauma. It might reflect that patients with abnormal MRI finding are more likely to deny their symptoms or have poor insight while patients with normal MRI finding have tendency to be preoccupied with or exaggerate psychiatric symptoms

References:

1. JK Lee: A Study on the Differences of the Psychiatric Symptoms between the Head Trauma Patients with CNS Lesions and without CNS Lesions in MRI Findings. J Korean Neuropsychiatr Assoc 1995;34:166-175.
2. Vanderploeg RD: Long-term neuropsychological outcomes following mild traumatic brain injury. J Int Neuropsychol Soc 2005; 11(3):228-236.

NR810 Wednesday, May 24, 3:00 PM - 5:00 PM

Non-Relapse Rate of Alcohol Dependence in a 24-Week Follow -Up Among Korean Male Patients

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize non-relapse rate of alcohol dependence in a 24 week follow-up among Korean male patients.

Summary:

Objective: To survey non-relapse rate of alcohol dependence from 24 weeks of OPD follow-up in Korean male patients with alcohol dependence.

Method: 48 males with alcohol dependence, 25 from 3 university hospitals, 18 from 2 general hospitals and 5 from 2 mental hospitals, were followed-up at OPD with Cognitive-Behavior Therapy and pharmacotherapy for 24 weeks. Inclusion criteria were DSM-IV diagnostic criteria, 15 or more Standard Drinks (SD)/week during 30 days before entry and at least one day/week of 5 SD or more/day. Exclusion criteria were significant physical diseases or conditions including acute hepatitis, significant psychotic conditions or disorders, substance dependence other than those with alcohol, nicotine and caffeine and history of prior treatment with disulfiram, naltrexone and acamprosate during last one year. Evaluation and treatment were performed at baseline, week 1, 2, 4, 6, 8, 10, 12, 16, 20 and 24. Treatments were Cognitive-Behavior Therapy based on the Project MATCH and pharmacotherapy with either naltrexone or acamprosate with an SSRI as needed. Evaluation of relapse was done based on materials obtained by Timeline Follow-Back which was performed at each follow -up session. Relapse was defined as either occurrence of a heavy drinking day with 5 SD or more/day or drop out.

Result and conclusion: Non-relapse rates were 47.9% at week 4, 29.2% at week 8 and 18.8% at week 24. If a non-relapse has been successful at week 8, the probability of maintaining sobriety until week 24 seemed to be considerably high.

References:

1. Project MATCH Research Group. Matching alcoholism treatments to client heterogeneity: Project MATCH secondary a priori hypotheses. Addiction. 1997;92:1671-1698.
2. Tonigan JS. Project Match treatment participation and outcome by self- reported ethnicity. Alcohol Clin Exp Res 2003;27:1340-1344.

NR811 Wednesday, May 24, 3:00 PM - 5:00 PM

Course of Major Depression in the Postpartum Period

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the need for a thorough risk/benefit analysis in the treatment of depression during pregnancy.

Summary:

Previous investigations have demonstrated that depression during pregnancy and a history of depression are significant risk factors for postpartum depression (PPD). The perinatal course of depression has been a major focus of our collaborative efforts. Remarkably, limited data has been generated on the course of depression across late pregnancy and postpartum or on the impact of antidepressant treatment.

A total of 155 pregnant women (<32 weeks gestation) with a history of MDD as determined by SCID were enrolled in a prospective study and followed through 6 months postpartum. Follow up visits included depression rating scales (BDI,HRSD) and SCID mood modules. Initial analysis employed a HRSD 17 item score of ≥ 15 to document depressive symptoms.

141 of the subjects completed the HRSD in late pregnancy and at ≥ 3 points postpartum. Of these, 107 were taking antidepressants proximate to delivery. Women were grouped by HRSD at 32-36 weeks (<15 and ≥ 15) and medication status (on and off). Not surprising, those with a HRSD≥ 15 in late pregnancy (n=25) had significantly higher rates of PPD (60%) compared to women with a HRSD<15 in late pregnancy (n=116)(28%).

Surprisingly, these preliminary data did not establish antidepressants as providing additional protection. Of women not taking antidepressants with a HRSD≥ 15 in late pregnancy (n=7), 57% relapsed postpartum while those with a HRSD<15 (n=27) had a 22% occurrence of PPD. Women taking antidepressants in pregnancy (n=107) with a HRSD≥ 15 (n=18) had a relapse rate of 61%

while those with a HRSD<15 during late pregnancy (n=89) had a rate of 29%.

Additional risk factors for PPD will be analyzed and discussed. Determination of relapse predictors, greatest window of risk, and optimal treatment strategies for women with a history of MDD entering the postpartum period is crucial to understanding the risk and benefits of treatment.

Supported by RO1-MH-063979

References:

1. O'Hara MW et al.: Controlled prospective study of postpartum mood disorders: psychological, environmental, and hormonal variables. J Abnorm Psychol 1991; 100: 63-73.

2. Stowe ZN et al.: The onset of postpartum depression: implications for clinical screening in obstetrical and primary care. American Journal of Obstetrics and Gynecology 2005; 192: 522-6.

NR812 Wednesday, May 24, 3:00 PM - 5:00 PM

Changes in Mental Health-Related Insurance Claims Costs Among Patients Treated for Bipolar Disorder

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Educational Objectives:

At the conclusion of the session, the participant should be able to compare the differences in mental health-related resource utilization among patients with bipolar disorder treated with different classes of psychotropic drugs.

Summary:

Objective: To evaluate pre- and post-treatment changes in mental health-related medical costs, emergency department (ED) visits, and inpatient admissions among adults with bipolar disorder (BPD) treated with different classes of psychotropic drugs.

Methods: Analysis of claims data from a large database of US employees. Patients with BPD were classified into those using: atypical antipsychotics only (ATYP); conventional antipsychotics and/or mood stabilizers only (OTHER); and both ATYP and OTHER medications (BOTH). Controlled regression models were utilized to evaluate changes in mental health-related outcomes after initiation of treatment.

Results: The adjusted reduction in mental health-related medical costs was significantly greater with ATYP (-$1,523, N=55) compared with BOTH (-$38, N=369, *P*=0.002) and OTHER (-$441, N=554, *P*=0.022). The ATYP group demonstrated a greater reduction (-11.5%) in mental health-related inpatient admissions than the OTHER group (-2.9%, *P*=0.076). The reduction in mental health-related ED visit rates for the BOTH group (-6.2%) was greater than for the OTHER group (-1.7%, *P*=0.008).

Conclusions: ATYP monotherapy for the treatment of BPD was associated with the greatest reduction in mental health-related medical costs, and combination therapy with other medications resulted in the greatest decrease in mental health-related ED visits. Thus, atypical antipsychotics play a significant role in the management of patients with BPD.

Supported by funding from AstraZeneca Pharmaceuticals LP.

References:

1. Stender M, Bryant-Comstock L, Phillips S: Medical resource use among patients treated for bipolar disorder: a retrospective, cross-sectional, descriptive analysis. Clin Ther 2002; 24:1668-1676.

2. Peele PB, Xu Y, Kupfer DJ: Insurance expenditures on bipolar disorder: clinical and parity implications. Am J Psychiatry 2003; 160:1286-1290.

NR813 Wednesday, May 24, 3:00 PM - 5:00 PM

Eszopiclone Co-Administered With Fluoxetine for Insomnia Co-Existing With MDD : Effects Following Eszopiclone Discontinuation

Andrew Krystal, M.D. *Duke University Medical Center, Trent Drive Box 3309, Durham, NC, 27710*, Robert Rubens, M.D., Maurizio Fava, M.D., Thomas Wessel, M.D., Thomas Roth, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to evaluate the effects of discontinuation of eszopiclone following eight weeks of concomitant treatment with eszopiclone and fluoxetine on measures of subjective sleep and depression severity.

Summary:

Objective: Insomnia and MDD may co-exist. The use of adjunctive hypnotics in this setting is controversial. We reported that eszopiclone/fluoxetine co-therapy significantly improved sleep and depression compared with fluoxetine monotherapy. Here we report data that further evaluated insomnia and MDD after discontinuation of eszopiclone due to concern that hypnotic discontinuation may undermine antidepressant response or hasten relapse.

Methods: Patients met DSM-IV criteria for MDD and insomnia. All patients received fluoxetine QAM for 10 weeks. Patients were randomized to eszopiclone 3mg (n=270) or placebo (n=275) QHS for 8 weeks, followed by a 2-week single-blind eszopiclone placebo discontinuation phase. During this discontinuation phase, subjective sleep was assessed daily; depression was assessed with the HAMD17 at the end of the phase (Week 10). Discontinuation effects were examined two ways: 1) change from baseline to Week 10; change from end of hypnotic treatment (EOT; Week 8) to Week 10.

Results: During the discontinuation phase, the eszopiclone group maintained significant sleep improvements observed over the first 8 weeks (Week 8-10 average $p<0.05$ versus placebo). Relative to baseline, patients discontinued from eszopiclone continued to have significantly improved sleep ($p<0.05$) at each daily assessment for SL, WASO, and TST (average change -124.0, -68.67, and 154.96 minutes, respectively). Relative to EOT, patients discontinued from eszopiclone did not show significant decrements over the 2 weeks for SL, WASO, or TST (average change 1.72, 1.6, and 0.59 minutes, respectively). Improvements in HAMD17 scores relative to placebo observed at EOT (-14.6 versus -12.3; $p=0.0005$) were maintained at Week 10 (-15.13 versus -12.70; $p<0.0001$).

Conclusions: In this study, sleep improvements associated with concomitant eszopiclone/fluoxetine were maintained after hypnotic discontinuation. Discontinuing eszopiclone was not associated with significant changes in measures of depression severity. No rebound insomnia was observed. Additional studies are needed to investigate the optimal duration of combination therapy.

Support: Sepracor

References:

1. Krystal AD, Walsh JK, Laska E, Caron J, Amato DA, Wessel TC, Roth T: Sustained efficacy of eszopiclone over 6 months of nightly treatment: results of a randomized, double-blind, placebo-controlled study in adults with chronic insomnia. Sleep 2003;.

2. Zammit GK, McNabb LJ, Caron J, Amato DA, Roth T: Efficacy and safety of eszopiclone across 6-weeks of treatment for

primary insomnia. Current Medical Research and Opinion 2004; 20(12):1979-1991.

NR814 Wednesday, May 24, 3:00 PM - 5:00 PM

Analysis of Individual Items of the Hamilton Depression Scale in a Study of Eszopiclone/ Fluoxetine Co-Therapy

Andrew Krystal, M.D. *Duke University Medical Center, Trent Drive Box 3309, Durham, NC, 27710*, Thomas Walsh, Ph.D., Maurizio Fava, M.D., Kendyl Schaefer, M.S.C., Thomas Roth, Ph.D., W. Vaughn McCall, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to evaluate the effects over time of concomitant treatment with eszopiclone and fluoxetine, versus fluoxetine alone, on the individual depression items assessed in the HAMD17.

Summary:

Objective: Results of a co-morbid insomnia and depression study of eszopiclone and fluoxetine demonstrated that initiation of co-therapy produced greater improvements in sleep and depression compared with fluoxetine monotherapy. To determine if the changes in the HAMD17 were due only to sleep, the individual HAMD17 items were evaluated.

Methods: Patients (n=545) met DSM-IV criteria for MDD and insomnia, with screening HAMD17 (excluding the sleep items) >14. All patients received fluoxetine QAM for 10 weeks, and randomly received double-blind eszopiclone 3mg or placebo QHS for 8 weeks, followed by a single-blind placebo 2-week run-out to evaluate discontinuation effects. HAMD17 was completed at Weeks 4, 8, and 10. Individual items were compared with ANCOVA using an LOCF approach.

Results: Mean baseline HAMD17 scores were 22 for each group. At Week 4, differences were noted between treatment groups in the total score, and the individual items of insight, and insomnia early, middle, and late ($p<0.02$ versus monotherapy), with a trend for guilt ($p=0.07$). At Week 8, significant changes were noted in the total score ($p=0.0005$), the three insomnia items ($p<0.001$), guilt, work/activities, and anxiety psychic ($p<0.05$), and a trend in retardation ($p=0.07$). At Week 10, the total score, guilt, insomnia early, middle, and late, work/activities, retardation, agitation, anxiety psychic, general somatic symptoms, and hypochondriasis demonstrated significant improvements ($p<0.05$ versus monotherapy) despite discontinuation of eszopiclone.

Conclusions: Eszopiclone/fluoxetine co-therapy resulted in significant improvements in the insomnia items of the HAMD17. In addition, several items related to core depressive symptoms were also improved with co-therapy compared with monotherapy, and these differences increased over time. Co-therapy led to an enhancement of the antidepressant response that was not sleep-specific but evident across the range of depression symptoms, and affected an increasing number of aspects of depression over time for at least 10 weeks.

Support: Sepracor Inc.

References:

1. Krystal AD, Walsh JK, Laska E, Caron J, Amato DA, Wessel TC, Roth T: Sustained efficacy of eszopiclone over 6 months of nightly treatment: results of a randomized, double-blind, placebo-controlled study in adults with chronic insomnia. Sleep 2003;.

2. Zammit GK, McNabb LJ, Caron J, Amato DA, Roth T: Efficacy and safety of eszopiclone across 6-weeks of treatment for primary insomnia. Current Medical Research and Opinion 2004; 20(12):1979-1991.

NR815 Wednesday, May 24, 3:00 PM - 5:00 PM

Ropinirole in Restless Legs Syndrome Requiring Extended Treatment Coverage

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Educational Objectives:

At the conclusion of this session, the participant should be able to recognize that some patients with Restless Legs Syndrome (RLS) may require extended treatment coverage and that ropinirole is an effective treatment in this population.

Summary:

Introduction: The dopamine agonist ropinirole, once daily, 1-3hrs before bedtime, is the only FDA-approved treatment for moderate-to-severe primary Restless Legs Syndrome (RLS).[1,2] Some patients, with symptom onset earlier in the day, may benefit from extended treatment coverage.

Methods: In this multicenter, double-blind, randomized, 12-week, flexible-dose study (protocol 101468/100013), patients with primary RLS, symptom onset no earlier than 5pm and baseline International Restless Legs Scale (IRLS) total score ≥20, received ropinirole (n=176), 0.5-6.0mg/day in divided doses, or placebo (n=187). First dose was 1hr before usual onset of symptoms and second was within 3-8hrs of the first. Efficacy assessments included change from baseline in IRLS total score (primary endpoint was at Week 12 last observation carried forward [LOCF]) and the proportion of responders (much/very much improved) on the Clinical Global Impression-Improvement (CGI-I) scale (secondary endpoint).

Results: Improvement in IRLS total score was statistically significantly greater for ropinirole compared with placebo at Day 3 observed case (OC) (adjusted mean treatment difference: -2.8; 95%CI: -4.5,-1.2; $p<0.001$) and Week 1 LOCF (-3.0; 95%CI: -4.6,-1.5; $p<0.001$) through Week 12 LOCF (-4.1; 95%CI: -6.1,-2.1; $p<0.001$). Additionally, a statistically significantly greater proportion of ropinirole-treated patients compared with placebo, were CGI-I responders at Day 3 OC (32% versus 15%; odds ratio [OR]: 2.6; 95%CI: 1.5,4.4; $p<0.001$) and Week 1 LOCF (39% versus 22%; OR: 2.2; 95%CI: 1.4,3.5; $p<0.001$) through Week 12 LOCF (71% versus 50%; OR: 2.4; 95%CI: 1.6,3.8; $p<0.001$). Ropinirole was generally well-tolerated. The adverse events reported by the most patients were nausea (34% versus 15%), headache (24% versus 18%), and somnolence (19% versus 6%), for ropinirole versus placebo, respectively.

Conclusions: Ropinirole, given in a divided dose, provides rapid, effective, and well-tolerated symptom relief for patients whose RLS requires extended treatment coverage.

Supported By: GlaxoSmithKline Research & Development.

References:

1. Trenkwalder et al. J Neurol Neurosurg Psychiatry 2004; 75: 92'7.

2. Walters et al. Mov Disord 2004; 19: 1414'23.

NR816 Wednesday, May 24, 3:00 PM - 5:00 PM

Ropinirole Improves Quality of Life in Patients With Restless Legs Syndrome Requiring Extended Treatment Coverage

Clete A. Kushida, M.D. *Stanford Center of Excellence for Sleep Disorders, 401 Quarry Road, Suite 3301-A, Stanford, CA, 94305-5730*, Jerry M. Tolson, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to understand the impact of Restless Legs Syndrome (RLS) on the

daily lives of patients and be familiar with the effects of ropinirole treatment on quality-of-life parameters in patients requiring extended treatment coverage.

Summary:

Introduction:

RLS often impacts negatively on patients' quality of life (QoL).[1] Once-daily ropinirole has been shown to improve RLS symptoms and, possibly as a result, QoL.[2] For patients whose symptom onset usually occurs during the late afternoon/early evening, extended treatment coverage may be required. Ropinirole's effect on QoL was examined in this population.

Methods:

Patients with primary RLS, baseline International Restless Legs Scale (IRLS) total scores ≥20, and symptom onset no earlier than 5pm received placebo or ropinirole, 0.5-6.0mg/day (titrated as needed and tolerated), in divided doses (first dose: 1h before usual symptom onset; second dose: 3-8h later) for 12 weeks (protocol: 101468/100013). The primary endpoint was the change from baseline to Week 12 in IRLS total score. Secondary efficacy assessments included the change from baseline to Week 12 in RLSQoL questionnaire overall life impact score and the proportion of patients satisfied/very satisfied when asked how satisfied they were with study medication.

Results:

The mean age in the intention-to-treat population (ropinirole= 175, placebo=184) was 50.9 (SD 13.4) years and 60% were women; the demographics were similar between treatment groups. The mean baseline IRLS score was 26.0 in both groups. The improvement in IRLS total score was statistically significantly greater with ropinirole than placebo at Week 12 last observation carried forward (adjusted mean treatment difference [AMTD]: -4.1; 95%CI: -6.1, -2.1; p<0.001), as was the improvement in RLSQoL questionnaire overall life impact score (AMTD: 7.9; 95%CI: 4.0, 11.8; p<0.001). A treatment difference favoring ropinirole was seen in the proportion of patients satisfied/very satisfied with treatment (Week 12 observed case; odds ratio: 2.8; 95%CI: 1.8, 4.4; p<0.001). The adverse-event profile for ropinirole was similar to that in once-daily-dosing studies.

Conclusions:

Ropinirole improved RLS symptoms and QoL, and was generally well tolerated in RLS patients requiring extended treatment coverage.

Supported by: GlaxoSmithKline Research & Development.

References:

1. Abetz L et al. Clin Ther 2004; 26: 925'935.

2. Walters AS et al. Mov Disord 2004; 19: 1414'1423.

NR817 Wednesday, May 24, 3:00 PM - 5:00 PM

The Eeffect of Smoking Cessation on EPS From Antipsychotics in Chronic Schizophrenic Patients

Tsuo-Hung Lan, M.D. *Yu-Li Hospital, DOH, Adult Psychiatry, 448 Chung-Hwa Road, Yu-Li, Hualien, 981, Taiwan Republic of China*, Hsien-Jane Chiu, M.D., Tsung-Ming Hu, M.D., Ching-Han Chao, M.D., Fan-Chin Kung, M.D., Huan Lee, M.D., Shih-Jie Wang, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize whether the side effects from antipsychotics change from the intervention of smoking cessation on schizophrenic patients.

Summary:

Objective: Smoking has been identified as a severe public issue worldwide since last century. Confirmed publications in the past emphasized the cause-effect relationship between smoking and many chronic diseases. More schizophrenic patients stayed on smoking compared to the general population, which indicates more quit-smoking campaigns should be promoted in this minor group.**Method:** This is a 3 year, investigator-initiated study project. Here we planed to enroll 500 inpatients meeting DSM-IV criteria for schizophrenia or schizoaffective disorder from a Taiwan based psychiatric hospital during the study. Patients were taking a variety of conventional and atypical antipsychotic medications with a confident compliance. All subjects after consent form completed were evaluated for side effects from antipsychotics by using UKU side effects scales at baseline and 4 weeks after Nicotine Transdermal Patch Treatment intervention. **Results:** After adjusted for age and hospitalization days, the change of UKU scale between baseline and 4 weeks later did not reach to a significant level. However, the 12th item (constipation) in UKU scale showed a significant difference before and after the Nicotine Transdermal Patch Treatment intervene (p-value = 0.02). **Conclusions:** This study indicates that schizophrenic patients might be beneficial in lessening side effects from antipsychotics through the smoking cessation intervention in Taiwan.

References:

1. Lerman C, Patterson F, Berrettini W.: Treating tobacco dependence: state of the science and new directions. J Clin Oncol. 2005; 23(2):311-23.

2. 2. Lerman C, Kaufmann V, Rukstalis M, Patterson F, Perkins K, Audrain-McGovern J, Benowitz N.: Individualizing nicotine replacement therapy for the treatment of tobacco dependence: a randomized trial. Ann Intern Med. 2004; 140(6):426-33.

NR818 Wednesday, May 24, 3:00 PM - 5:00 PM

Armodafinil Reduces Sleepiness in Chronic Shift Work Sleep Disorder

Alan Lankford, Ph.D. *Sleep Disorders Center of Georgia, 5505 Peachtree Dunwoody Road, Suite 380, Atlanta, GA, 30342*, Gary Zammit, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that armodafinil reduces excessive sleepiness and consequences associated with chronic shift work sleep disorder during the night shift and the commute home.

Summary:

Introduction/Hypothesis: Shift work sleep disorder (SWSD) is associated with excessive sleepiness (ES) at night and insomnia during the day. The effects of the wake-promoting agent, armodafinil on sleepiness during the night shift and the commute home in patients with ES associated with chronic SWSD are reported.

Methods: This 12-week, double-blind, placebo-controlled multicenter study in permanent or rotating night shift workers with chronic SWSD evaluated armodafinil 150 mg (n=112) or placebo (n=112) before the start of each night shift. Patients completed daily electronic diaries in which they recorded sleepiness, number of mistakes/near misses/accidents, and caffeine use, during the night shift and on the commute home.

Results: Armodafinil significantly reduced the mean number of unintended sleep episodes (percent reduction, 71.8%) and naps (percent reduction, 35.8%) compared with placebo (percent reduction, 42.2% and 13.2%, respectively; $P \leq .05$). Armodafinil significantly improved the level of alertness versus placebo during the night shift (decrease of sleepiness from baseline 2.0 versus 1.1 points; $P < .0001$) and the commute home (decrease of sleepiness from baseline 1.2 versus 0.6 points; $P = .0027$). The mean number of mistakes/near misses/accidents during the night shift and on the

commute home was lower for the armodafinil group than placebo, although it did not achieve statistical significance. The change from baseline in the use of caffeinated drinks was relatively unchanged in both groups.

Conclusions: Armodafinil significantly reduced patients' estimates of sleepiness during the night shift and the commute home.

Funding Source: Sponsored by Cephalon, Inc.

References:

1. Drake CL, Roehrs T, Richardson G, et al: Shift work sleep disorder: prevalence and consequences beyond that of symptomatic day workers. Sleep 2004; 27:1453-62.
2. Barger LK, Cade BE, Ayas NT, et al: Extended work shifts and the risk of motor vehicle crashes among interns. N Engl J Med 2005; 352:125-34.

NR819 Wednesday, May 24, 3:00 PM - 5:00 PM

Haloperidol Versus Risperidone in the Treatment of Aggressive Psychotic Male Inmates

Catherine F. Lewis, M.D. *University of Connecticut Health Center, Psychiatry, 263 Farmington Avenue, Farmington, CT, 06030-2103*

Educational Objectives:

At the conclusion of this presentation, the participant should recognize and be able to compare the efficacy of haloperidol versus risperidone for the treatment of aggressive inmates with psychotic disorders.

Summary:

Objective: To examine the relationship of treatment with risperidone versus haloperidol to aggression in psychotic male inmates.

Method: This study took place at Osborn Correctional Institution in Somers, Connecticut on a specialized mental health housing unit for inmates with serious mental illness. Forty male prisoners with Axis I psychotic disorder (diagnosed with the Diagnostic Interview Schedule for DSM IV (DIS)) were randomized to one of two treatment arms of ninety days each. One arm (N=20) received risperidone (dose initiation of 2 mg PO daily with weekly titration of 2 mg up to therapeutic maximum of 6mg daily) and the other arm (N=20) received haloperidol (dose initiation of 4 mg daily with weekly titration of 2 mg PO daily up to therapeutic maximum of 12 mg daily). Patients on mood stabilizers were not eligible for the study. The primary measure of aggression was the Overt Aggression Scale-Modified (OAS-M), which was administered weekly. Trait impulsivity was assessed with the Barratt Impulsivity Scale (BIS), which was administered at initiation and conclusion of the study.

Results: Haloperidol and risperidone were both associated with reduced aggression as evidenced by significant decreases in each subscale of the OAS-M. A trend toward a significant drug by subgroup interaction was seen; specifically risperidone was associated with greater reductions in OAS-M overall scores in individuals with higher (>73) scores on the baseline BIS ($p<0.07$). Compliance did not differ between the two study arms.

Conclusion: Haloperidol and risperidone showed similar efficacy in reducing state aggression in psychotic male inmates. There was a trend, which approached statistical significance, for patients with higher baseline scores of impulsivity to have more significant reductions in state aggression with risperidone. Further research with larger samples is needed to more fully explore this finding.

References:

1. Yudofsky SC, Silver JM, Jackson W, Endicott J, Williams D: The Overt Aggression Scale for the objective rating of verbal and physical aggression. Am J Psychiatry 1986; 143: 35-39.
2. Hollander E, Swann AC, Coccaro EF, Jiang P, Smith TB: Impact of trait impulsivity and state aggression on divalproex versus placebo response in borderline personality disorder. Am J Psychiatry 2005; 162: 621-624.

NR820 Wednesday, May 24, 3:00 PM - 5:00 PM

MAO-B Activity in Platelets Associated With Suicide Attempts in Depressed Patients

Ute Lewitzka, M.D. *University of Dresden, Psychiatry, ulewi@web.de, ulewi@web.de, Dresden, 01307, Germany*, Bruno Mueller-Oerlinghausen, Prof. Dr., Erik Lauterbach, M.D., Markus Ising, M.D., Wolfgang Maier, Prof. Dr., Marie-Luise Rao, Prof. Dr., Thomas Bronisch, Prof. Dr.

Educational Objectives:

We found a correlation of higher platelet activity with circumstances in a way that increased the possibility of fatal exit which support the hypothesis that characteristics of suicide attempts may be associated with a lower 5-HT availibility.

Summary:

Introduction:

The objectives of the present study is to investigate neurobiological parameters of serotonergic, noradrenergic and dopaminergic transmitters and aspects of suicidality.

Methods:

After suicide attempts (within 14 days) platelets serotonergic measures were obtained from 89 patients (32 men, 27 women) suffering from an "affective spectrum" disorders and from 30 non-suicidal patients (14 men, 16 women). Subjects were recruited in 5 participating centers. The patients were screened for the exclusion criteria e.g. having other psychiatric disorder or use of prohibited medication. Behavioral assessments were done as soon as possible after the suicide attempt. Blood sampling for measurement of platelet MAO-B acitivity, platelet 5-HT content and platelet 5-HT2A receptor acitivity was done mostly on the same day as the psychological assessments (on average 13,2 days after suicide attempt)

Results:

Patient with suicide attempt did not differ from patients without history of suicide attempts in age or in gender distribution. Major depression was the most important diagnosis in both groups. Suicide attempters and non suicide attempters were not different in depressive and anxiety symptoms as well as general psychopathology.

Suicide attempters who arranged the circumstance of their suicide attempt in a way that increased the likelihood of a fatal exit, showed higher platelet MAO-B acitivity suggesting lower 5-HT availability.

Discussion:

We found a correlation of higher platelet activity with circumstances in a way that increased the possibility of fatal exit which support the hypothesis that characteristics of suicide attempts may be associated with a lower 5-HT availibility.

References:

1. Journal Article - Bronisch T: A multicenter Study about Neurobiology of Suicidal Behavior: Design, Development and Preliminary Results. Archives of Suicide Res 2005; 9:19-26.
2. Journal Article: Mueller-Oerlinghausen B: Serotonergic platelet markers of suicidal behavior-do they really exist? Journal of Affective Disorders 2004; 79: 13-24.

NR821 Wednesday, May 24, 3:00 PM - 5:00 PM

Increased Proliferation of Blood Peripheral Lymphocytes of Major Depression Patients and the Role of $5HT_{1A}$ Receptors

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Educational Objectives:

The objectives of the present research were:

1. To explore the nervous-immune interaction in major depression patients
2. To determine basal proliferation of lymphocytes in major depression
3. To understand the role of serotonin in the process of lymphocyte proliferation thinking in autoimmunity and depression
4. To evaluate populations of lymphocytes with differential function and the serotonergic system
5. To highligth the relevance of possible immune modifications an the treatment of depression
6. To train Residents in New Research

Summary:

Depressed present reduced lymphocyte proliferation to mitogens. Lymphocyte $5HT_{1A}$ receptors are unmodified in depressed, modulate cAMP levels, which inhibits proliferation. We studied 29 patients, 18-56 years, 7 men, and 30 controls, 21-59, 10 men. Diagnosis was done according to DSM-IV criteria and severity by Hamilton Scale of Depression (28-32). Blood lymphocytes, by Ficoll/Hypaque and plastic adherence, cultured in RPMI medium 72 h without or with Concanavalin A (CONA). 5HT, 8-hydroxy-dipropil-aminotetralin (DPAT) or WAY-100635, agonist and antagonist of $5HT_{1A}$ receptors, imipramine or fluoxetine, were added. CD4+ (helper/inducer), CD8+ (cytotoxic), and 5HT transporter positive cells were immunolabeled. Basal proliferation was higher in depressed, without effect of CONA. DPAT increased and WAY-100635 decreased proliferation in depressed. Imipramine and fluoxetine decreased it. CD4+/CD8+ ratio was unchanged, 50% CD4+ and 30% CD8+; 20% had 5HT transporter, reduced in patients, present in 25% of CD4+ and in 45% of CD8+. Lymphocytes are activated, and $5HT_{1A}$ hiper-reactive in depressed. Differential localization of 5HT transporter might indicate variable role of 5HT in populations of lymphocytes from depressed.

References:

1. Fajardo O, Galeno J, Urbina M, Carreira I. Lima L. Serotonin, serotonin 5-HT1A receptors and dopamine in blood peripheral lymphocytes of major depression patients. Int Immunopharmacol 2003, 3:1345-1352.
2. Mizrahi C, Stojanovic A, Urbina M, Carreira I, Lima L. Differential cAMP levels and serotonin effects in blood peripheral mononuclear cells and lymphocytes from major depression patients. Int Immunopharmacol 2004, 4:1125-1133.

NR822 Wednesday, May 24, 3:00 PM - 5:00 PM

The Use of Complementary and Alternative Medicine Among Menopausal Women With Mood Problems

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Educational Objectives:

Complementary and alternative therapy (CAM) in menopausal-related mood women

Summary:

Background: Hot flash and menopausal symptoms can be troublesome, especially when hormone therapy (HT) is contraindicated. The use of complementary and alternative medicine (CAM) is common among our patients to treat their menopausal symptoms by themselves. To understand this health-seeking behavior is necessary for the quality of health-care.

Method: The present study was conducted from December 2004 to May 2005, a total of 95 women who sought treatment for menopause-related problem at our special clinic. All were recruited with informed consent. Each patient completed a questionnaire that identified demographic data, height and weight, family and personal history, and medical and gynecological history. Information about the use of CAM was collected in another special questionnaire.

Result: The majority of the subjects were married (76.8%) and housewives (70.5%) with the mean age were 52.6 $\pm$ 6.2 years. The mean year of education was 8.6 $\pm$ 3.7 years. 85.3% of them had used CAM within 6 months before our clinics. The average usage of CAM was 3.00 $\pm$ 2.67 kinds and this was statistically significant with the level of education ($P<0.05$). The ranking of CAM used were calcium (43.2%), isoflavone (38.9%), Magnet-oencephalographic avitamin (32.6%), specific milk powder for menopausal women (30.5%), vitamin E (25.3%), glucosamine sulfate (16.8%), fish oil (13.7%), cranberry (12.6%), ginkgo (11.6%), and vitamin C (11.6%). 48.4% of them had used Traditional Chinese Medicine (TCM). The majority of TCM was OTC (over the counter) drug (27.4%), followed by prescribed by doctor (22.1%), chiropractic or foot massage (16.8%), and acupuncture (12.7%).

Conclusion: Individuals chose CAM may not because of dissatisfaction with conventional medicine, but alternative therapies were more congruent with their personal beliefs and values. Physician cannot always be disinterested in or threatened by alternative medicine approaches. Quality control of CAM may be our responsibility for completed human-care in the future.

References:

1. Geller SE: Botanical and dietary supplements for menopausal symptoms: what works, what does not.J Womens Health 2005; 14:634-649.
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NR823 Wednesday, May 24, 3:00 PM - 5:00 PM

Gaboxadol Improves Sleep Maintenance and, in Contrast to Zolpidem, Enhances Slow Wave Sleep in Adult Patients With Primary Insomnia

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Educational Objectives:

The participants will gain knowledge on the effect of Gaboxadol on the sleep maintenance and slow wave sleep in patients with primary insomnia.

Summary:

Introduction: Gaboxadol is a selective extrasynaptic Gamma-aminobutyric acid $_A$ agonist (SEGA) in development for the treatment of insomnia. This study was designed to evaluate its acute efficacy and safety in the treatment of primary insomnia (PI).

Methods: This was a randomised, double-blind, 4-way cross-over, polysomnograph (PSG) study comparing gaboxadol 10mg (GBX10) and 20mg (GBX20) to placebo (PBO) in 40 adult patients

with PI. Zolpidem 10mg (ZOL10) was used as an active reference drug. Treatment was administered on two consecutive nights in each treatment session. Patients were enrolled after confirmation of DSM-IV criteria for PI and specific PSG inclusion criteria for sleep onset and maintenance. Next day residual effects were evaluated 2h after lights on.

Results: The per protocol efficacy analysis (n=38) was based on data from the second night of each treatment session. Both gaboxadol doses and ZOL10 significantly reduced wakefulness after sleep onset (all $p<0.05$, log transformed). GBX20 and ZOL10 increased total sleep time (all $p<0.05$). Both doses of gaboxadol but not zolpidem, reduced the number of night awakenings ($p<0.001$). Neither drug reduced sleep onset latency. Gaboxadol dose dependently enhanced slow wave sleep (SWS; $p<0.01$ for GBX10 and GBX20). Neither drug treatment was associated with next day residual effects the morning after treatment. The majority of adverse events (AEs) were mild or moderate with no SAEs. Compared to placebo, the incidence and severity of AEs were higher with GBX20.

Conclusion: Acute administration of gaboxadol improves sleep maintenance and enhances SWS in a dose dependent manner in adult patients with PI. Effects on sleep induction need further evaluation considering the lack of effect of the reference drug zolpidem. Gaboxadol 10mg and 20mg doses were not associated with next day residual effects. Gaboxadol was generally well tolerated although gaboxadol showed a dose dependent increase in incidence and severity of AEs.

References:

1. Storustovu S, Ebert B. Gaboxadol: in vitro interaction studies with benzodiazepines and ethanol suggest functional selectivity. Eur J Pharmacol. 2003 Apr 25;467(1-3):49-56.
2. Deacon, S., Staner, L., Staner C., Vorstrup, S. and Lundahl J. Acute administration of gaboxadol improves sleep initiation and maintenance in patients with primary insomnia [abstract]. Sleep, Vol 28, 2005.

NR824 Wednesday, May 24, 3:00 PM - 5:00 PM

Serotonin Transporter Gene and Moderators of Prolactin Response to Meta-Chlorophenylpiperazine in African American Cocaine Abusers and Controls

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Educational Objectives:

At the conclusion of this presentaiton, the participant should be able to understand the interaction of genetic and psychobehavioral dimensions in determining the functional response to drug abuse.

Summary:

Introduction 5HT (5-HT) function is altered in several psychiatric disorders, including cocaine dependence (CD), and its role in impulsive aggressive behaviors has been widely studied. However, the relationship between psychopathological and behavioral dimensions and mechanisms of 5-HT alterations remains unclear. **Methods** We investigated the relationship of a polymorphism in the 5' promoter region of the 5HT transporter gene (5-HTTLPR) with prolactin (PRL) response to meta-chlorophenylpiperazine (m-CPP) in a sample of 68 African American individuals, 35 CD subjects and 33 controls. We also examined whether measures of impulsivity, hostility and sensation-seeking influenced the relationship between 5-HTTLPR polymorphism and PRL response to m-CPP in this sample. **Results** Individuals with the SS genotype showed heightened PRL response to the challenge compared to the LL and LS genotypes ($F=4.40_{2,64}$; $p=0.016$). No influence of gender or substance abuse condition was observed. Hostility was associated with blunted PRL response in the total sample ($F=2.19_{1,66}$, $p=0.023$). Cocaine abuse was the most significant moderator of ΔPRL (peak PRL-baseline PRL), and the interaction of genetic, behavioral and psychopathological measures helped predict most of the observed ΔPRL (62,5%). **Conclusions** Although these results need replication, variation in 5-HTTLPR gene appears to influence measures of 5-HT function and interact with disease state and personality dimensions to account for 5-HT disturbances in African American populations.

References:

1. Buydens-Branchey L, Branchey M, Fergeson P, Hudson J, McKernin C (1997). The meta-chlorophenylpiperazine challenge test in cocaine addicts: hormonal and psychological responses. Biol Psychiatry 41: 1071-1086.
2. Broocks A, Briggs NC, Pigott T, et al. (1997): Behavioral, physiological and neuroendocrine responses in healthy volunteers to m-chlorophenylpiperazine (m-CPP) with and without ondansetron pretreatment. Psychopharmacology.

NR825 Wednesday, May 24, 3:00 PM - 5:00 PM

Eszopiclone Co-Administered With Fluoxetine for Insomnia Co-Existing With MDD: Analysis by Age

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to evaluate the effect of co-therapy with eszopiclone and fluoxetine, versus fluoxetine alone, in patients of different ages with co-existing insomnia and depression.

Summary:

Objective: Results of a study of eszopiclone and fluoxetine in co-existing insomnia and depression showed initiation of co-therapy produced greater improvements in sleep and depression compared with fluoxetine monotherapy. Results of a post-hoc analysis of results by age are presented.

Methods: Patients (aged 21 - 64 years) met DSM-IV criteria for MDD and insomnia, with screening 17-item Hamilton Depression Rating Scale (HAMD-17; excluding the sleep items) >14. All patients received fluoxetine QAM for 10 weeks. Patients were randomized to eszopiclone 3mg (n=270) or placebo (n=275) QHS for 8 weeks, followed by a 2-week single-blind placebo run-out phase. Sleep and depressive symptom responses were evaluated in younger (<50 years; n=351) and older adults (≥50 years; n=136).

Results: At baseline, older adults had greater difficulty with sleep indicated by longer sleep latency (SL), greater wake time after sleep onset (WASO) and less total sleep time (TST) compared with younger adults. Sleep quality, daytime alertness, and ability to function and concentrate in younger adults were either better or the same as in older adults. Both age groups responded to eszopiclone/fluoxetine with statistically differences relative to fluoxetine alone in SL ($p\leq0.0042$), WASO ($p\leq0.0215$) and TST ($p\leq0.052$). Those in the older age group had greater changes in these parameters. Change from baseline HAMD-17 scores in the younger versus older group, respectively, were -12.01 versus -11.67 for co-therapy and -10.34 versus -8.95 with monotherapy. The percentage of responders (≥50% decrease in HAMD-17 score) was 59% versus 65.8% in the younger versus older group, respectively (monotherapy: 49.2% and 52.2%, respectively). Similarly, the percentage of remitters (HAMD-17 scores ≤7) was 42.9% versus 46.3% in the younger and older group (monotherapy: 36.1% and 31.9%), respectively.

Conclusions: In this study, regardless of age, co-therapy provided significant improvements in both sleep and depression endpoints relative to monotherapy.

Support: Sepracor Inc.

References:

1. Krystal AD, Walsh JK, Laska E, Caron J, Amato DA, Wessel TC, Roth T: Sustained efficacy of eszopiclone over 6 months of nightly treatment: results of a randomized, double-blind, placebo-controlled study in adults with chronic insomnia. Sleep 2003;.
2. Zammit GK, McNabb LJ, Caron J, Amato DA, Roth T: Efficacy and safety of eszopiclone across 6-weeks of treatment for primary insomnia. Current Medical Research and Opinion 2004; 20(12):1979-1991.

NR826 Wednesday, May 24, 3:00 PM - 5:00 PM

Prevalence of PTSD in Pregnant Women With Previous Pregnancy Complications

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Educational Objectives:

At the conclusion of this presentation, the participant will be aware of the incidence of PTSD in pregnant women who have experienced a prior pregnancy complication. In addition, clinicians will become familiar with a method to assess pregnant women with previous pregnancy complications for PTSD.

Summary:

Objective: PTSD involves the development of characteristic symptoms following a traumatic event, including re-experiencing the event, avoidance of stimuli associated with the event, and symptoms of increased physiologic arousal. As a pregnancy loss or other complication can be considered traumatic and severity of PTSD has been linked to the frequency of traumatic reminders, we sought to examine the prevalence of full and partial PTSD in a group of pregnant women who have experienced a previous pregnancy loss or serious complication.

Methods: Forty-two pregnant women referred to a university-based maternal fetal medicine program who experienced a previous pregnancy loss or complication completed a self-rated pregnancy complication questionnaire (PCQ) based on the Clinician-Administered PTSD Scale (CAPS-1). Another 24 women underwent a clinical interview to assess presence of PTSD due to a pregnancy-related trauma.

Results: Of the 42 women who provided self-rated assessments, the prevalence of PTSD meeting DSM-IV criteria was 5/42, while an additional 10/42 met criteria for partial PTSD. Of the 24 women who underwent clinician-rated assessments, 2/24 met criteria for full PTSD and 6/24 met criteria for partial PTSD.

Conclusions: The prevalence of full and partial PTSD in women who are pregnant subsequent to a pregnancy-related trauma is considerable. Given anxiety during pregnancy is not without risks to both mother and fetus, women who have experienced a previous pregnancy loss should be screened for the presence of clinically meaningful symptoms of PTSD.

References:

1. Blake DD, Weathers FW, Nagy LM, Kaloupek DG, Gusman FD, Charney DS, Kean TM: The Development of a Clinician-Administered PTSD Scale. J Traum Stress 1995; 8:75-90.
2. Blanchard EB, Hickling EJ, Taylor AE, et al: Effects of varying scoring rules of the Clinician-Administered PTSD Scale (CAPS) for the diagnosis of post-traumatic stress disorder in motor vehicle accident victims. Behav Res Ther 1995; 33:471-475.

NR827 Wednesday, May 24, 3:00 PM - 5:00 PM

Psychotropic Drug Use and Recidivism Among High Need and High Risk Sex Offenders

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Educational Objectives:

To identify reasons for psychotropic drug use in paraphilia and sex offences

To understand the role of psychotropics in reducing sexual recidism

Summary:

Objective

1. To determine the indications and benefits of prescribing psychotropic medications among recidivist sex offenders.

2. To estimate the recidivism rates among those prescribed psychotropic medications and those who are not.

Method: Data on indications and benefits of psychotropic medications in 365 high need/high risk sex offenders was compared with the yearly sexual and violent recidivism rates for those released (85% of sample).

Results: There is an increase in the use of SSRIs in this population over the years. Mood, anxiety disorders and personality characteristics like impulsivity and insomnia are the main psychotropic drug indications. Sexual recidivism rates at two, three and five years (4.2 %, 4% and 12.1%) amongst those prescribed SSRIs and anti-libidinal drugs are lower than those on no medication. Those prescribed medications for sexual deviance had the lowest rate of sexual recidivism over five years (0%).

Conclusion: With increasing use, the SSRIs and anti-libidinal drugs offer a significant reduction in sexual recidivism when prescribed for paraphilia and for other mood and anxiety problems. Specific pharmacological treatment of sexual deviance is associated with the lowest sexual recidivism rate.

References:

1. Bradford JMW: The neurobiology, neuropharmacology and pharmacological treatment of the paraphilias and compulsive sexual behaviour. Can J Psychiatry 2001; 46:26-34.
2. Nicholaichuk T, Gordon A, Gu D, Wong S: Outcome of an institutionalsexual offender treatment program: A comparison between treated and matched untreated offenders. Sexual Abuse: A journal of research and treatment 2000 12(2): 139-153.

NR828 Wednesday, May 24, 3:00 PM - 5:00 PM

The Efficacy of Lamotrigine in the Treatment of Women With Chronic Pelvic Pain and Depression

Samantha E. Meltzer-Brody, M.D. *University of North Carolina, Psychiatry, Campus Box 7160, Chapel Hill, NC, 27599*, Jane Leserman, Ph.D., Katherine Rinaldi, B.A., Denniz Zolnoun, M.D., John Steege, M.D.

Educational Objectives:

Educational Objectives:

Understand the relationship between chronic pelvic pain and mood symptoms.

Describe preliminary data on the anticonvulsant lamotrigine in the treatment of chronic pelvic pain and depression.

Summary:

Objective: Chronic Pelvic Pain (CPP), defined as pelvic pain of least 6 months duration, is a common disorder characterized by heterogeneous symptoms, poor treatment response, high relapse rates, and psychiatric symptoms. Lamotrigine is an anticonvulsant with demonstrated efficacy in mood stabilization and promising data on treatment of neuropathic pain. Our goal was to examine the efficacy of lamotrigine for the treatment of CPP and associated mood symptoms.

Method: We recruited women from a tertiary care referral based clinic for CPP for inclusion in an open-label 14-week pilot study of lamotrigine. After the baseline assessment, patients were titrated up to a therapeutic dose of 400mg of lamotrigine over 8 weeks. This maintenance dose was then continued from week 8-12, and then patients were gradually discontinued from the drug between weeks 12-14. Patients completed the McGill Pain Scale at each visit, and were administered the Hamilton Depression and Anxiety Scales.

Results: In our preliminary analysis of 14 patients who completed at least 8 weeks of study, the average age was 43.0 (SD= 11.6), and average education was 14.9 years (SD=2.0). There was a statistically significant change in overall reduction of pain intensity at 8 weeks (p=0.0004) and 12 weeks (p=0.04) compared to the baseline visit. In addition, there was a trend for the group to have reductions in measures of depressive symptoms from baseline to 12 weeks (p=.09). Patients with vulvodynia-type pelvic pain (N=6) tended to have the most robust reductions on pain intensity from baseline to 8 (p=.003) and 12 weeks (p=.005) compared patients with other types of CPP (e.g., diffuse abdominal pain).**Conclusions:** Our preliminary data suggest that lamotrigine may have a clinically significant effect on the reduction of pain and depressive symptoms in women with CPP, particularly among those with vulvodynia-type pelvic pain.

Funded by GSK

References:

1. Mathias SD, Kuppermann M, Liberman RF, Lipschutz RC, Steege JF: Chronic pelvic pain: prevalence, health-related quality of life, and economic correlates. Obstet Gynecol 87(3):321-7, 1996.

2. Jamieson DJ, Steege JF: The association of sexual abuse with pelvic pain complaints in a primary care population. Am J Obstet Gynecol 177: 1408-12, 1997.

NR829 Wednesday, May 24, 3:00 PM - 5:00 PM

OREON 2: Impact of an Educational Program for Physicians on Remission Rates in Depression

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Educational Objectives:

The "Objective REmission in DepressiON" project OREON 1 had shown that remission rates in depressed patients in daily practice are low . An internet based interactive training on remission in depression was offered to the OREON 1 investigators. OREON 2 assessed remission in newly treated patients after the training phase. The presented data will demonstrate that a well developped educational program for physicians can improve remission rates.

Summary:

Objective: Evaluation of impact of an educational intervention on remission in patients treated for depression.

Method: The "Objective REmission in DepressiON" project OREON 1 had shown that remission rates in depressed patients are low in daily practice. An internet based interactive training on remission in depression was then offered to the OREON 1 investigators. OREON 2 assessed remission in newly treated patients after the training phase. Investigators included 10 consecutive patients with depression. Symptom severity was evaluated by means of HAM-D 7 (GP) or HAM-D-17 (psychiatrist). Comorbidity and impact of disease on social functioning was evaluated by means of the Physicians Health Questionnaire (PHQ), the Sheehan Disability Scale (SDS) and the Carroll scale

The effect of the training program was tested by: (1) comparison of remission rates in OREON 1 and OREON 2; (2) correlation between remission rate and amount of training received by the physician and (3) comparison of remission rates obtained in both studies within each practice individually.

All statistical results will be considered significant at the 5% critical level ($p<0.05$). All calculations will be performed using SAS (version 8.2 for Windows) and S-PLUS (version 6.1).

Results: In OREON 2 **remission rates in primary care have increased to 50% compared to 28% in OREON 1.**

The OREON project is funded by Wyeth Pharmaceuticals Belgium. The internet based educational program was developped by Prof Degryse at the Academic Center of Primary Care Medicine.

References:

1. Keller, MB, 2003. Past, present and future directions for defining optimal treatment outcome in depression. Remission and Beyond. JAMA, 289: pp. 3152-3160.

2. McIntyre, R., Kennedy, S., Bagby, M., Bakish, D., 2002. Assessing full remission. J Psychiatry Neurosci ;27(4): pp. 235-9.

NR830 Wednesday, May 24, 3:00 PM - 5:00 PM

Quetiapine Augmentation of Antidepressants in Lactation: Breastmilk Levels and Infant Development

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to: treat women with concurrent psychiatric disorders during lactation, understand quetiapine augmentation of antidepressants in lactation, and be familiar with the effects of combination therapy on infant development.

Summary:

Objective: To further knowledge regarding the effects of quetiapine as an augmenting agent of antidepressants, specifically, venlafaxine, trazodone, or paroxetine, during lactation. The secretion of these medications in breastmilk and developmental assessments of the exposed babies are reported.

Method: Participants included six breastfeeding women referred to a tertiary care clinic for treatment of psychiatric disorders in Vancouver, Canada. All patients were diagnosed with MDD in conjunction with Panic Disorder, Obsessive Compulsive Disorder, or BPD, and treated with quetiapine in combination with either an SSRI or SNRI postnatally. Breastmilk samples were examined to determine levels of psychotropic medications and estimate levels of infant exposure. Developmental assessments of the exposed babies were performed with the Bayley Scales of Infant Development, Second Edition (BSID-II).

Results: In half of the cases, no medication was detected in the breastmilk, and in all but one case, estimated levels of infant medication exposure were less than 0.01 mg/kg/day for each medication. Four babies scored within normal limits on the BSID-II, while two showed mild developmental delays. In comparison to the four cases of typical development, the two showing mild delays did not have higher estimated levels of psychotropic medication exposure through breastmilk.

Conclusions: Although our results should be interpreted with caution, in our limited sample there appears to be no association between developmental functioning of babies up to 18 months of age and estimated levels of exposure. Women who are on a combination of psychotropic medications and choose to nurse need to be monitored closely. When pharmacotherapy is utilized to ensure stability of maternal mood during lactation, monitoring developmental milestones in infants is recommended whenever possible.

References:

1. Lee A, Giesbrecht E, Dunn E, Ito S: Excretion of quetiapine in breast milk. Am J Psychiatry 2004; 161(9):1715-1716.
2. Misri S, Milis L: Obsessive-compulsive disorder in the postpartum: open-label trial of quetiapine augmentation. Journal of Clinical Psychopharmacology 2004; 24(6):624-627.

NR831 Wednesday, May 24, 3:00 PM - 5:00 PM

The Influence of Religious Affiliation on Time to First Treatment and Hospitalization

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Educational Objectives:

At the conclusion of this program, participants will be able to: Understand the the importance of the duration of untreated psychosis; Recognize that religious affliation may influence the path to care; Conceptualize future research involving the relationship of religion and psychiatric treatment.

Summary:

Longer duration of untreated psychosis (DUP) has been associated with treatment-refractory illness, significant cognitive decline, and poorer long-term outcomes. There are many factors, including social and cultural, that promote longer DUP. To date, there have been no studies to evaluate religion's effect on DUP. In this study we evaluated the effect of certain religious affiliations and degree of religious practice on the DUP. *Methods:* A total of 195 patients were recruited aged 18 to 45 years with the presence of at least 1 psychotic symptom (delusions, hallucinations, or prominent thought disorder). Patients were evaluated on their religious practice prior to the index episode using a Likert-style scale. Using a similar scale, patients were asked about their religious affiliation categorized as Catholic, Protestant, or none at all. *Results*: Correlational analysis revealed that the time to first treatment and time to first hospitalization were both was negatively related to degree of religious practice ($r = -.15$, $N = 161$, $p < .05$ and $r = -.18$, $N = 161$, $p < .05$ respectively). Between-group comparisons revealed longer DUP in the Protestant group compared to the no affiliation and Catholic groups ($p = .05$).*Conclusion:* From our results, it appears that the degree of religious practice does not affect length of time to treatment in psychotic patients. However, having a Protestant religious affiliation is strongly associated with having a greater delay in treatment seeking for psychosis. Factors contributing to a longer DUP in this group warrant further study.

References:

1. Bottlender, R., Sato, T., Jager, M., Wegener, U., Wittmann, J., Strauss, A., Moller, H.J., 2003. The impact of the duration of untreated psychosis prior to first psychiatric admission on the 15-year outcome in schizophrenia. Schizophrenia Resear.
2. Drake, R.J., Haley, C.J., Akhtar, S., Lewis, S.W., 2000. Causes and consequences of duration of untreated psychosis in schizophrenia. British Journal of Psychiatry. 177, 511-515.

NR832 Wednesday, May 24, 3:00 PM - 5:00 PM

Predicting Outcomes of Treatment to Restore Competence to Stand Trial

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Educational Objectives:

After viewing this presentation, the participant should be able to describe or recognize factors that predict whether a defendant who is incompetent to stand trial has an above- or below-average likelihood of regaining competence if provided with a course of treatment.

Summary:

Objective: In the U.S., courts frequently require forensic examiners to offer opinions concerning the likelihood that criminal defendants found incompetent to stand trial can be "restored" through treatment. Yet no jurisdiction has established legal guidelines for testimony concerning restorability, and scientific publications suggest that mental health professionals cannot accurately predict whether treatment to restore competence will succeed. This study asked whether reliable information that is consistently available to forensic examiners might support empirically grounded opinions about the likelihood of restoration.

Methods: Using records from all 351 patients who underwent competence restoration at a state psychiatric hospital in 1995-99, we evaluated whether several types of information that are reliable and consistently available to forensic examiners--including evaluees' demographic characteristics, diagnoses, symptom patterns, criminal charges, number of prior hospitalizations, and cumulative prior length of stay (LOS)--would predict treatment outcome. We modeled the probability of successful restoration using logistic regression equations, and evaluated the equations' predictive accuracy using *k*-fold cross-validation and receiver operating characteristic (ROC) analysis.

Results: Lower probability of restoration was associated with having a misdemeanor charge, longer cumulative LOS, older age, and diagnoses of mental retardation, schizophrenia, and schizoaffective disorder. Although the overall rate of successful restoration for felony defendants was 75 percent, logistic equations allowed selection of subgroups with high probabilities of restoration (>90 percent) and low probabilities of restoration (<30 percent). In cross-validation simulations, predictive equations had ROC areas of 0.728 for all defendants, and 0.746 for felony defendants.

Conclusions: Our findings provide scientific support for testimony that two types of incompetent evaluees have well-below-average probabilities of being restored: chronically psychotic defendants with histories of lengthy inpatient hospitalizations, and defendants whose incompetence stems from unremediable cognitive disorders (such as mental retardation). Nonetheless, courts may still deem low probabilities of success to be "substantial" enough to warrant attempts at restoration.

References:

1. Pinals DA: Where two roads meet: restoration of competence to stand trial from a clinical perspective. New Eng Journal on Criminal & Civil Confinement 2005; 31:81-108.
2. Nicholson RA, Barnard GW, Robbins L, Hankins G: Predicting treatment outcome for incompetent defendants. Bull Am Acad Psychiatry Law 1994; 22:367-77.

NR833 Wednesday, May 24, 3:00 PM - 5:00 PM

Starting Dose and Persistence for Five Major Atypical Antipsychotic Agents Among Medicaid Enrollees

C. Daniel Mullins, Ph.D. *University of Maryland, Pharmaceutical Health Services Research, 515 West Lombard Street, 2nd Floor, Baltimore, MD, 21201*, Nour Obeidat, M.S., John Naradzay, B.S.

Educational Objectives:

To determine the relationship between starting dose of atypical antipsychotic drugs in general and persistence among patients diagnosed with schizophrenia, and to evaluate this relationship at a drug-specific level.

Summary:

Methods: Adult Medicaid recipients diagnosed with schizophrenia and having prescription claims for any of the major atypical antipsychotic drugs (aripiprazole, olanzapine, quetiapine, risperidone and ziprasidone) between 7/1/01 and 9/30/03 were categorized by starting dosage as low dose or high dose patients. Persistence was measured using refill patterns, allowing 14-day gaps between expected refill dates. For the five major drugs pooled together (n=3523), multivariate Cox proportional hazards regression analysis then explored the impact of low versus high starting dose of antipsychotic, controlling for age, gender, race, hospitalization prior to initiation of drug therapy, and concurrency in psychotropic medications. The analysis was then repeated for each of the atypical antipsychotics separately. Finally, a sensitivity analysis was conducted allowing a 29 day gap between prescriptions in defining discontinuation.

Results: In the combined analysis of all atypicals, starting on a high dose was significantly associated with a lower hazard of discontinuation (HR=0.872 p=0.0045). When the drugs were considered separately, using a 14 day gap to define discontinuation, this significant association persisted only for ziprasidone (HR= 0.808, p=0.0191). When the 14 day gap was extended to 29 days in the sensitivity analysis, a significant association remained between high doses of ziprasidone and lower discontinuation rates and ziprasidone (HR=0.758, p=0.0040). In addition, the same relationship was also observed for olanzapine (HR=0.831, p= 0.0140), risperidone (HR=0.791, p=0.0287).

Conclusions: In contrast to other antipsychotics, persistence with ziprasidone is generally higher when patients are initiated on a high dose versus low dose. This association, although apparent in the pooled analysis, was not consistent when other atypical drugs were examined separately. Results are consistent with a prior study among commercially insured Ziprasidone users.

References:

1. Keith SJ, Kane JM. Partial compliance and patient consequences in schizophrenia: our patients can do better. J Clin Psychiatry. Nov 2003;64(11):1308-1315.
2. Gilmer TP, Dolder CR, Lacro JP, et al. Adherence to treatment with antipsychotic medication and health care costs among Medicaid beneficiaries with schizophrenia. Am J Psychiatry. Apr 2004;161(4):692-699.

NR834 Wednesday, May 24, 3:00 PM - 5:00 PM

Efficacy of Lamotrigine for Bipolar Disorder in Pregnancy

D. Jeffrey Newport, M.D. *Emory University School of Medicine, Psychiatry, 1365 Clifton Rd NE, Suite 6100, Atlanta, GA, 30322*, Sandra Juric, B.A., Martha R. Calamaras, B.S., James Ritchie, Ph.D., Page B. Pennell, M.D., Adele C. Viguera, M.D., Zachary N. Stowe, M.D.

Educational Objectives:

At the conclusion of this presentation, the participation should be able to recognize the comparative rate and time to recurrence for pregnant women receiving continued lamotrigine therapy versus those who discontinue mood stabilizer therapy due to safety concerns.

Summary:

The management of bipolar disorder (BPD) during pregnancy remains one of the most daunting challenges of modern psychiatry. Most psychotropic agents used to manage BPD possess either significant teratogenic potential or limited reproductive safety data. Consequently, it is common practice to discontinue mood stabilizer therapy during organogenesis; however, untreated pregnant women with BPD experience high relapse rates. Lamotrigine is unique among mood stabilizers in that published pregnancy registry data suggests it does not increase the risk for major malformations and thereby may be safe for first trimester administration. The objective of this study was to compare the relapse rates for women with BPD who continue lamotrigine therapy to those who discontinue mood stabilizer therapy at knowledge of conception.

Survival analysis was conducted for 15 women fulfilling DSM-IV diagnostic criteria for BPD who at conception were euthymic and receiving mood stabilizer therapy. Weekly clinical global impression (CGI) scores were determined prospectively across gestation. Six women received continuous lamotrigine therapy. Nine women discontinued mood stabilizer therapy at knowledge of conception (lamotrigine n=3; lithium n=3; valproate n=3). All 6 women receiving continuous lamotrigine therapy remained euthymic (CGI≤2) throughout gestation. None of the 9 women who discontinued mood stabilizer therapy remained euthymic. Time to relapse was 6.6±5.5 weeks after medication discontinuation. Peak CGI scores were 1.8±0.4 during pregnancy for those continuing mood stabilizer therapy and 3.9±0.8 for those discontinuing therapy.

These data suggest that continuous mood stabilization with lamotrigine during pregnancy may be not only safe but effective as well. Additional relapse predictors including psychosocial factors and comorbidity will be examined.

References:

1. Cunningham M, Tennis P, et al. Lamotrigine and the risk of malformations in pregnancy. Neurology 2005;64:955-960.
2. Yonkers KA, Wisner KL, Stowe Z, et al. Management of bipolar disorder during pregnancy and the postpartum period. Am J Psychiatry 2004;161:608-620.

NR835 Wednesday, May 24, 3:00 PM - 5:00 PM

Impaired Sleep-Related Memory Consolidation in Primary Insomnia: A Pilot Study

Christoph Nissen, M.D. *University of Pittsburgh Medical Center, Western Psychiatric Institute and Clinic, 5850 O'Hara Street, Pittsburgh, PA, 15213*, Corinna Kloepfer, Eric Allen Nofzinger, M.D., Dieter Riemann, Ph.D., Mathias Berger, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to describe the actual clinical and preclinical knowlegde of the impact of normal sleep on the consolidation of memories. Furthermore, the participant should be able to discuss possible impairments of sleep-related memory consolidation in patients with primary insomnia.

Summary:

Preclinical and clinical evidence indicates that sleep can contribute to the consolidation of memories. In the present pilot study, we investigated the pre-post sleep consolidation of procedural memory traces in 7 patients with primary insomnia compared to

7 gender, age and IQ matched healthy controls. Polysomnography did not reveal a significantly disturbed sleep profile in the patient compared to the control group (MANOVA: $F(10,3) = 8.7$, $p = 0.050$, univariate tests not significant). Pre-sleep performance in a mirror tracing task did not differ significantly between the groups. Both groups performed significantly better in the post-sleep recall session (MANOVA for repeated measurement factor test session: $F(9,4) = 31.8$, $p = 0.000$). However, healthy controls showed an improvemt of 42.8 ± 5.8 % in the mirror tracing draw time, whereas patients with insomia showed only an improvement of 20.4 ± 14.8 % (MANOVA test session * group interaction: $F(9,4) = 10.9$, $p = 0.002$). These findings support the view that the sleep-associated consolidation of procedural memories may be impaired in patients with primary insomnia.

References:

1. Plihal W, Born J: Effects of Early and Late Nocturnal Sleep on Declarative and Procedural Memory. J.Cogn.Neurosci. 1997; 9:534-547.
2. Walker MP, Stickgold R: Sleep-dependent learning and memory consolidation. Neuron 2004; 44:121-133.

NR836 Wednesday, May 24, 3:00 PM - 5:00 PM

Reducing Inpatient Aggression: Paying Attention Pays Off

Karen A. Nolan, Ph.D. *Nathan S. Kline Institute for Psychiatric Research, 140 Old Orangeburg Road, Orangeburg, NY, 10962*, Leslie L. Citrome, M.D., Kohta Saito, Jimmy Xu

Educational Objectives:

At the conclusion of this presentation the participant should be able to recognize that training staff to more accurately report aggressive behaviors may offer a means of reducing the frequency of physically aggressive incidents as among psychiatric inpatients.

Summary:

Researchers interested in understanding and treating aggressive behavior face a difficult challenge in accurately detecting, describing, and classifying the behavior in question. Although inpatient settings provide our highest level of care, much of the aggressive behavior that occurs is not reported, or is reported inaccurately. Video surveillance can be helpful but because many aggressive incidents last only seconds, detection remains difficult and is extremely labor-intensive. A 9-camera video recording system has been in operation on the Secure Unit of the Clinical Research and Evaluation Facility at the Nathan Kline Institute since 1999. All video recorded during a one-month period in 2000 was systematically reviewed. Comparison to official reports revealed that 22.5% of the 71 aggressive incidents viewed on tape had not been reported. Subsequent interventions to improve reporting focused on the therapy aides, whose work entails direct contact with patients on the unit. The same procedures were used during the corresponding one-month period in 2005 to replicate the previous review. The results revealed no significant change in the number of aggressive incidents on the CREF, but a significant improvement in reporting: 95.2% of the 62 events detected in 2005 had been reported. There were also significant changes in the types of aggressive behavior, with a reduction in physical aggression and an increase in verbal aggression. These results suggest that interventions that encourage staff to report aggressive behavior may have the unanticipated benefit of reducing physical aggression.

References:

1. Crowner ML, Peric G, Stepcic F, Van Oss E: A comparison of videocameras and official incident reports in detecting inpatient assaults. Hosp Community Psychiatry 1994;45:1144-1145.
2. Nolan KA, Czobor P, Roy BB, Platt MM, Shope CB, Citrome LL, Volavka J: Characteristics of assaultive behavior in psychiatric inpatients. Psychiatric Services 2003;54:1012-1016.

NR837 Wednesday, May 24, 3:00 PM - 5:00 PM

Management of Comorbid Insomnia in Psychiatric Patients: A Survey Conducted on Italian Psychiatrists

Paolo Pancheri *University of Rome "La Sapienza", Rome, Italy, Department of Psychiatry, via Tacito 90, Rome, 00185, Italy*, Mario Giovanni Terzano, Fabio Cirignotta, Luigi Ferini-Strambi, Alessandro Rossi, Giovanni Muscettola

Educational Objectives:

Chronic insomnia is usually comorbid with psychiatric and physical disorders.

To evaluate the approach to psychiatric patients with sleep problems, a questionnaire was proposed to 5,000 Italian psychiatrists covering homogeneously the national territory.

A specifically designed questionnaire was prepared by a panel of six specialists. A total of 48 items were submitted to the Italian psychiatrists.

Available results derived so far from 510 completed questionnaires indicate that: I) 82.2% of the interviewed psychiatrists addresses the patient to a sleep specialist only if insomnia is associated with another sleep disorder; II) psychiatrists consider benzodiazepines as the drugs that more often cause EEG alterations; III) anxiety generalized disorder is considered as the anxiety disorder more frequently associated with sleep disorders; IV) most psychiatrist consider insomnia as the most frequent symptom preceding depression and the most frequent residual symptom after depression improvement; V) 53% expect insomnia to remain after an manic episode.

For Italian psychiatrists insomnia is difficult to manage only when associated with other sleep disorders.

They indicate anxiety generalized disorder as frequently comorbid with sleep disorders and consider insomnia as a pivotal symptom in the evolution of depression and manic episodes.

Summary:

Introduction. Chronic insomnia is usually comorbid with psychiatric and physical disorders. Two Italian epidemiological surveys (Studio Morfeo 1 and Studio Morfeo 2) provided information on the frequency and management of insomnia in the primary care setting. In the case of comorbidity, the risk of insomnia was higher in the patients who suffered from depressive symptoms. To evaluate the approach to psychiatric patients with sleep problems, a questionnaire was proposed to 5,000 Italian psychiatrists covering homogeneously the national territory.

Methods. A questionnaire was prepared by a panel of six specialists indicated be the Italian Association of Sleep Medicine and the Italian Society of Psychopathology. A total of 48 items were submitted to the Italian psychiatrists to investigate their general knowledge of sleep and their opinion on the diagnostic and therapeutic management of insomnia in patients with sleep disorders concomitant with psychiatric diseases (subdivided into anxiety disorders, mood disorders and schizophrenia).

Results. Available results derived so far from 510 completed questionnaires indicate that: I) 82.2% of the interviewed psychiatrists addresses the patient to a sleep specialist only if insomnia is associated with another sleep disorder; II) psychiatrists consider benzodiazepines as the drugs that more often cause EEG alterations (68.8% versus 8.4% for non-benzodiazepine hypnotics); III) anxiety generalized disorder is considered as the anxiety disorder more frequently associated with sleep disorders (67.7%); IV) most psychiatrist consider insomnia as the most frequent symptom preceding depression (45.5%) and the most frequent residual symp-

tom after depression improvement (28%); V) 53% expect insomnia to remain after an manic episode.

Conclusions. For Italian psychiatrists insomnia is difficult to manage only when associated with other sleep disorders. They indicate anxiety disorders as frequently comorbid with sleep disorders and consider insomnia as a pivotal symptom in the evolution of depression and manic episodes.

References:

1. Terzano MG, Parrino L, Cirignotta F, Ferini-Strambi L, Gigli G, Rudelli G, Studio Morfeo Committee: Studio Morfeo: insomnia in primary care, a survey conducted on the Italian population. Sleep Med 2004; 5:67-75.
2. Leger D, Poursain B: An international survey of insomnia: under-recognition and under-treatment of a ploysymptomatic condition. Curr Med Res Opin 2005; 21:1785-1792.

NR838 Wednesday, May 24, 3:00 PM - 5:00 PM

Coping Styles in Prodromes of Bipolar Mania

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Educational Objectives:

At the conclusion of this presentation, participants should be able to:

(i) identify several validated coping strategies used to cope with bipolar mania prodromes

(ii) note the differences in preferred coping strategies between Bipolar I and Bipolar II subtypes

(iii) become familiar with a useful instrument for measuring coping with manic prodromes and ascertain its utility and validity.

Summary:

Objective: To examine the Coping Inventory for Prodromes of Mania (CIPM) in bipolar disorder (BD) both for validity and utility in understanding coping styles as a key mechanism in the efficacy of psychosocial interventions. The CIPM is organized into four factors of coping including: *stimulation reduction (SR), problem-oriented coping (PR), seeking professional help (SPH), denial and blame (DB).*

Method: 203 bipolar patients, recruited from across Canada for a clinical trial comparing psychoeducation to Cognitive-Behavior Therapy, completed a CIPM at baseline. CIPM psychometric properties and its relationship to demographic and clinical factors, dysfunctional attitudes, and mood symptoms were examined. Finally, post hoc coping profiles were generated by BD subtype (I versus II).

Results: Internal consistencies and subscale means were commensurate with the original validation study. Neither demographic/clinical characteristics nor mood symptoms showed any particular relationship with the CIPM; however, the CIPM was related to dysfunctional attitudes. Clear differences in coping also emerged between BD I and BD II subjects. BD I tended to use a wider range of coping strategies and scored highly on the SPH factor as compared to BD II subjects. BD II participants preferred to use DB and PR, but were less likely to use SPH and Sustained Release .

Conclusion: The CIPM appears to be a valid measure of coping despite indications that two subscales demonstrated less than adequate internal consistency. Canadian norms appear consistent with a previously published study. Coping style preferences appear to differ according to bipolar subtype.

References:

1. Wong G, Lam, D: The development and validation of the coping inventory for prodromes of mania. Journal of Affective Disorders 1999; 53: 57-65.
2. Lam D, Wong G, Sham P: Prodromes, coping strategies and course of illness in bipolar affective disorder--a naturalistic study. Psychological Medicine 2001; 31:1397-1402.

NR839 Wednesday, May 24, 3:00 PM - 5:00 PM

A Survey of Attitudes Around Depression Among African Americans at a Community Event

Kavita K. Patel, M.D. *UCLA/RAND, 1776 Main Street, PO Box 2138, Santa Monica, CA, 90407*, Susan Stockdale, Ph.D., Delores Hill, M.S.W., Ruthie Gray, Loretta Jones, M.A., Kenneth B. Wells

Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand the process involved in the development of a community based participatory survey and also understand the diverse perspectives around the impact of depression and substance use in the community. Specifically, the participant should have an enhanced understanding of the roles of unemployment, traffic, noise, homelessness and police brutality can have on mental health.

Summary:

Introduction and Purpose: Over the next decade depression is expected to become the leading cause of disability in developed economies of the world, owing to its strong impact on morbidity and relatively high prevalence across the lifespan, with relatively early age of onset. In order for mental health stakeholders to be able to understand how to deal with such a significant condition, innovative mechanisms of community engagement should be explored in order to focus efforts on approaches which are culturally appropriate and relevant for consumers. This community questionnaire is aimed to explore such issues.

Methods and Results: A 16 item questionnaire was distributed to a convenience sample of 1405 participants at a community event in South Los Angeles. The questionnaire items were developed through a participatory community based approach in which academic and community partners develop hypotheses, objectives and questions around the specific aims of a research project. This questionnaire explored the relationship between depression, substance use and other community contextual variables such as noise, traffic, policy brutality and unemployment with a goal of understanding the priorities of a community in terms of mental health policy directives. Of the 1405 respondents, 984 were African American. Overall, 48.82% of the sample (n=680) stated that they personally knew someone with depression. For each of the contextual variables, including violence, abandoned buildings, traffic and graffiti, over half of the respondents felt that the variables contributed strongly to mental health disorders and substance use in their community.

Conclusions: African Americans in our community are very concerned about the problems which both exacerbate as well as result from mental health and substance use disorders. Future research should explore community based participatory approaches to minimizing the negative impact of these issues by coupling policy relevant measures with outcomes

References:

1. MacAulay AC: Participatory Research Maximizes Community and Lay Involvement. British Medical Journal 1999; 319: 744-748.
2. Israel BA: Review of Community Based Research. American Journal of Public Health 1998; 19: 173-202.

NR840 Wednesday, May 24, 3:00 PM - 5:00 PM

Suicidality in Body Dysmorphic Disorder: A Prospective Study

Katharine A. Phillips, M.D. *Butler Hospital/Brown University, 345 Blackstone Boulevard, Providence, RI, 02906*, William Menard, B.A.

Educational Objectives:

The educational objective of this poster is to learn about suicidality in body dysmorphic disorder. Suicidality is a topic of very high clinical relevance which has been very understudied in this relatively common disorder.

Summary:

Objective: Cross-sectional/retrospective data indicate that individuals with BDD have high rates of suicidal ideation and attempts. However, no study has prospectively examined suicidality in BDD. *Methods*: In the first prospective naturalistic observational study of BDD's course, we examined suicidality in 183 broadly ascertained subjects for up to 3 years (mean of 2.1 [SD=0.8] years) of follow-up. *Results*: Suicidal ideation was reported by 56.7% (95% CI, 51.5% - 61.8%) of subjects per year (annual weighted mean). A mean of 2.8% (95% CI, 1.1% - 4.5%) attempted suicide per year. Two subjects completed suicide (0.6% [95% CI, -0.2% - 1.3%] per year). *Conclusions*: Individuals with BDD have very high rates of suicidal ideation and attempts. The annual suicidal ideation rate of 56.7% is approximately 10-25 times higher than in the U.S. population, and the annual suicide attempt rate of 2.8% is 4-13 times higher. The completed suicide rate is very preliminary but suggests that the rate of completed suicide is markedly high. This very high completed suicide rate is consistent with findings that individuals with BDD have many suicide risk factors. Studies are needed that examine suicidality over a longer follow-up period and in other BDD samples.

References:

1. Phillips KA, Coles M, Menard W, Yen S, Fay C, Weisberg RB: Suicidal ideation and suicide attempts in body dysmorphic disorder. J Clin Psychiatry 2005; 66:717-725.
2. Phillips KA, Menard W: Suicidality in body dysmorphic disorder: a prospective study. Am J Psychiatry, in press.

NR841 Wednesday, May 24, 3:00 PM - 5:00 PM

Dopamine D2 and Serotonin 5-HT1A Receptors Polymorphisms: Towards a Dual Genetic Modulation of Alcohol Craving

Emmanuel B. Pinto, M.D. *Universite de Liege, Psychiatry, Chu Sart Tilman B35, Liege, 4000, Belgium*, Philip Gorwood, M.D., Jean Reggers, Ph.D., William Pitchot, M.D., Marc Ansseau, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be aware that genetic differences may influence alcohol craving

Summary:

Introduction.

Significant association has been reported between DRD2, substance misuse and craving. 5HT is also thought to play a predominant role in alcoholism. We studied the links between alcohol craving and both the A1 allele of the DRD2 and the C-1019 allele of the 5-HT1A receptor.

Methods.

60 male alcohol dependent patients were hospitalized for withdrawal. Craving was monitored weekly throughout their 4-week stay and twice in 2 months after discharge, using the OCDS. Genomic DNA was extracted and PCR amplifying Taq1a polymorphisms of the DRD2 and C-1019G polymorphisms of the 5-HT1A receptor were performed. The impact of DRD2 (A1 or A2 alleles) and 5-HT1A (C or G alleles) on craving was assessed by ANOVAs.

Results.

Craving was significantly higher during acute withdrawal in homozygous patients for the C1019 allele of the 5-HT1A receptor ($p = .002$). The A1 allele of the DRD2 didn't influence craving during hospitalization but two months after discharge, abstinent patients carrying the A1 allele exhibited higher craving scores than homozygous patients for the A2 allele ($p = .004$).

Conclusions.

Alcohol craving may be influenced by genetic differences in alcohol dependent patients. There seems to be a dual serotonergic and dopaminergic modulation of craving. During acute withdrawal, desire to drink is predominantly influenced by the C1019 allele of the 5-HT1A receptor. Conversely, carrying the A1 allele of the DRD2 increases craving only when patients are no longer hospitalized and protected from drinking cues.

References:

1. Heinz A et al.: Correlation betweenDopamine D2 receptors in the ventral striatum and central processing of alcohol cues and craving. Am J Psychiatry 2004; 161: 1783-1789.
2. Alcohol dependence and polymorphisms of serotonin-related genes. Med Sci 2004; 20 : 1132-1138.

NR842 Wednesday, May 24, 3:00 PM - 5:00 PM

Safety Assessment of Long-Term Ramelteon Use in Subjects With Chronic Insomnia

Gary S. Richardson *Henry Ford Hospital, 2799 W Grand Boulevard CFP - 3, Detroit, MI, 48202*, Sherry Wang-Weigand, Jeffrey Zhang, Michael DeMicco

Educational Objectives:

At the conclusion of this presentation, the participant should be able to describe the safety of ramelteon in adults and older adults with chronic insomnia.

Summary:

Introduction: The long-term safety of the chronohypnotic ramelteon, a highly selective MT_1/MT_2-receptor agonist, was evaluated in subjects with chronic insomnia.

Methods: Subjects (N=1213) diagnosed with chronic insomnia (DSM-IV-TR criteria) and reporting symptoms for at least 3 months received ramelteon nightly for 1 year followed by a 3-day placebo run-out. Subjects 65 years or older received ramelteon 8mg (n= 248); those 18 to 64 years received ramelteon 16mg (n=965). Safety was assessed at monthly clinic visits over the course of the study.

Results: Of 1213 subjects, 597 completed 6 months and 473 completed 1 year of treatment. Early discontinuation was primarily due to lack of efficacy (19.7%), adverse events (AEs) (12.2%), and consent withdrawal (11.9%). After 1 year, the AEs occurring most frequently with ramelteon 8mg and 16mg were nasopharyngitis (10.5% and 14.9%), somnolence (9.5% and 8.1%), upper respiratory tract infection (7.6% and 11.1%), headache (1.9% and 13.5%), and sinusitis (1.9% and 7.8%). Overall, AEs were primarily mild or moderate and occurred at a similar frequency at 6 months and 1 year. Of 38 subjects (3.1%) reporting a serious AE, only 3 AEs were considered possibly treatment related. There were no clinically meaningful changes in vital signs, physical exams, clinical chemistry, hematology, or urinalysis values over 1 year of ramelteon administration. No notable changes in multiple measures of endocrine function and sexual/reproductive function were observed except for slight mean decreases in testosterone (free and total) in older men (8mg), which returned to normal by the Final Visit. There were no ECG trends to suggest adverse effects

on cardiac conduction or rhythmicity with long-term ramelteon treatment.

Conclusion: Long-term ramelteon treatment was well tolerated and did not adversely affect safety measures.

References:

1. Kato K, Hirai K, Nishiyama K, et al: Neurochemical properties of ramelteon (TAK-375), a selective MT1/MT2 receptor agonist. Neuropharmacology 2005; 48:301-310.
2. Zammit G, Roth T, Erman M, Sainati S, Weigand S, Zhang J: Double-blind, placebo-controlled polysomnography and outpatient trial to evaluate the efficacy and safety of ramelteon in adult patients with chronic insomnia [abstract]. Sleep 2005; 28:A22.

NR843 Wednesday, May 24, 3:00 PM - 5:00 PM

Birth Order, Maternal Age and Birth Weight as Risk Factors for Suicide in Later Life

Daniel V. Riordan *NHS Highland, (Scotland), Psychiatry, New Craigs, Leachkin Road, Inverness, IV3 8NP, United Kingdom*, Cameron Stark, M.B., Sivasubramaniam Selveraj, M.S.C.

Educational Objectives:

At the conclusion of this presentation, the participants should be able to understand the association demonstrated in this large Scottish birth cohort, between early adult suicide and maternal parity, maternal age and birth weight.

They should be able to appreciate the very significant potential public health implications, especially of the findings on young motherhood.

They should also be able to consider some of the potential mechanisms for these associations. These include;

Attachment theory,

Maternal nutritional deficiencies, Maternal-fetal origins hypothesis; (Exposure to high cortisol levels in utero, induced by maternal stress.)

and *Parental underinvestment theory* (An anthropological model of differential parental treatment of offspring according to birth order.)

Summary:

To examine the association between perinatal circumstances and subsequent suicide in Scotland.

Higher birth order has been associated with self-harm, but not suicide. In one previous study, (not yet replicated), a higher risk of suicide was found to be associated with low birth weight, as well as with being the offspring of a teenage mother.

Method

The Scottish morbidity record is a population based dataset which includes maternity records on births since 1969. These records include data on mother's age, occupation and previous pregnancies, as well as infant's birth weight and gestational age at birth. These records were linked, using probability matching, to Scottish death records, which include data on cause of death. A birth cohort of 1,061,830 people was followed up for a mean of 26.7 years. Data was analysed using a Cox regression analysis.

Results

A significant association was found between maternal parity and offspring suicide. Compared with first borns, individuals born to women with one or two previous completed pregnancies, were more likely to have died by suicide, with a hazard ratio (HR) = 1.6, ($p < 0.001$). For 3 or more previous pregnancies, this HR increased to 2.68, ($p< 0.001$).

Younger maternal age (<25 years), non-professional parental occupations and very low birth weight (<1750g) were also independently associated with higher risk.

Conclusion

Our results suggest a birth order effect on suicide. Possible mechanisms for this include the maternal-fetal origins (of affective disorders) hypothesis, maternal nutritional deficiencies, attachment theory, and parental underinvestment theory.

The effects of birth order and young motherhood, on offspring suicidal behaviour, are potentialy of major public health significance.

Declaration of Interests

None.

The study was funded by the Scottish Chief Scientist's Office.

References:

1. Miitendorf-Rutz E, Rasmussen F, Wasserman D: Restricted Fetal Growth and Adverse Maternal Psychosocial and Socioeconomic Conditions as Risk Factors for Suicidal Behaviour of Offspring: A Cohort Study. Lancet 2004; 364: 1135-1140.
2. O'Keane V, Scott J: From /obstetric complications' to a maternal'foetal origin hypothesis of mood disorder. Brit J Psych; 2005; 186: 367-368.

NR844 Wednesday, May 24, 3:00 PM - 5:00 PM

Risk Factors and Symptoms of PTSD in Women Veterans With PTSD: Is Race a Factor?

E. Joyce Roland, Ph.D. *VA Medical Center/DUMC/NCCU, Psychiatry/Mental Health, VAMC/Women's Health, 508 Fulton Street, Durham, NC, 27705*, Jennifer L. Strauss, Ph.D., Marian I. Butterfield, M.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to:

(a) Summarize risks factors for PTSD in women veterans with PTSD;

(b) Determine if trauma exposure in women veterans differs by race and sociodemographic factors;

(c) Determine if lifetime prevalence of trauma patterns and PTSD severity (as measured by PCL), differ by race in women veterans;

(d) Compare PTSD symptoms and symptoms clusters in African American and Caucasian women veterans by race.

Summary:

Objective: To examine racial differences in victimization patterns and posttraumatic stress disorder symptoms in women veterans.

Methods: A sample of 200 women veterans in a VA mental health clinic enrolled in the study. The sample included Caucasian and African American women with PTSD (N=131). A validated risk interview was administered assessing lifetime victimization, exposure to community violence, sociodemographic characteristics and PTSD symptoms. Bivariate analyses were performed to determine if PTSD symptom clusters, lifetime victimization, and exposure to community violence differed by race.

Results: Forty-four percent of the women were African American and 55.7% were Caucasian. Racial differences in trauma exposure were noted. Caucasian women reported higher rates of childhood physical assault than African American women (68.4% versus 51.2%; $p<0.05$). High rates of physical and sexual assault, and community violence existed with no between group differences.

Conclusion: The two groups of women veterans appear more alike in their patterns of victimization and PTSD symptom severity. Treatments strategies based on awareness of lifetime victimization patterns of both groups of veterans are warranted.

References:

1. Butterfield, M.I., Becker, M. & C. Marx. Posttraumatic stress disorder in women: current concepts and treatments. Current Psychiatric Reports. 2002:474-486.

2. Ruiz, P. Addressing Culture, Race and Ethnicity in Psychiatric Practice. Psychiatric Annals, 2004:34 (7):527-532.

NR845 Wednesday, May 24, 3:00 PM - 5:00 PM

Long-Acting Injectable Risperidone Versus Zuclopenthixol in the Treatment of Schizophrenia With Substance Abuse Comorbidity

Gabriel Rubio, Ph.D. *Complutense University of Madrid, Spain, Psychiatry, Lope de Rueda, 43, Eboli,24,4,a, Madrid, 28050, Spain*, Isabel Martinez-Gras, Ph.D., Guillermo Ponce, Ph.D., Miguel Angel Jiménez-Arriero, Ph.D., Francisco López-Muñoz, Ph.D., Cecilio Alamo, Prof. Dr.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to treat subjects with schizophrenia and substnce abuse comorbidity

Summary:

Substance use disorders (SUDs) are present in more than 50% of subjects diagnosed with schizophrenia. However, there are no controlled studies assessing the efficacy of antipsychotic drugs in this subgroup of patients. The objetive of the present study was to compare the efficacy of long-acting risperidone and zuclopenthixol in subjects with schizophrenia and substance abuse. At the same time we aimed through this comparation to determine which antupsychotic drug would improve symptoms of schizophrenia and produce better compliance with the psychotherapeutic programme for reducing or ceasing substance use.

Method: A hundred and fifteen subjects with schizophrenia and SUDs were enrolled for an open, randomized, controlled, 6-mont-follow-up study.

Fifty-seven subjects were selected for treatment with long-acting injectable risperidone, while another fifty-eight were treated with zuclopenthixol-depot. Substances most commonly used were alcohol (87%), cannabis (71%) and cocaine (26%). Psychopathological and clinical scales were used every two months. Participants received training on how to reduce their consumption of substances (Substance Abuse Management Module, SAMM).

Results: Long-acting risperidone group patients presented fewer positive urine tests (8.67 versus 10.36, p=0.005), improved their scores on the PANSS and showed better compliance with the SAMM programme. Using long-acting risperidone and less severe dependence explained outcome at the end of the follow-up.

Conclusions: Long-acting injectable risperidone was more effective than zuclopenthixol-depot in improving substance abuse and symptoms of schizophrenia in subjects with dual diagnosis. Atypical antipsychotics could be the best pharmacological strategy in the treatment of subjects with schizophrenia and substance abuse comorbidity.

References:

1. Dixon L. Dual diagnosis of substance abuse in schizophrenia: prevalence and impact on outcomes. Schizophr Res 1999; (Supp 35): 93-100.

2. Smelson DA, Losonczy MF, Davis CW, Kaune M, Williams J, Ziedonis D. Risperidone decreases craving and relapses in individuals with schizophrenia and cocaine dependence. Can J Psychiatry, 2002; 47:671-675.

NR846 Wednesday, May 24, 3:00 PM - 5:00 PM

Ropinirole Improves Restless Legs Syndrome (RLS) Symptoms and Sleep in RLS Patients With Periodic Leg Movements

David B. Rye, M.D. *Emory University School of Medicine, 101 Woodruff Circle, WMRB Suite 6000, Atlanta, GA, 30322*, Nancy L. Earl, M.D.

Educational Objectives:

At the conclusion of this session, the participant should understand the effects of ropinirole, a dopamine agonist, on objective (periodic leg movements during sleep measured using actigraphy) and subjective symptoms of Restless Legs Syndrome (RLS) (measured using the International Restless Legs Scale) as well as associated sleep benefits (measured using the Medical Outcomes Study Sleep Scale).

Summary:

Introduction: Sleep problems are common among patients with Restless Legs Syndrome (RLS) and likely result both from RLS *per se* and also from periodic leg movements during sleep (PLMS) that affect at least 80% of RLS patients.[1,2] Quantitative measures of PLMS (by actigraphy) and subjective measures of RLS symptoms (International Restless Legs Scale, IRLS) and sleep (Medical Outcomes Study [MOS] Sleep Scale Sleep Problems Index II) were examined in a subpopulation of RLS patients with PLMS.

Methods: In the TREAT RLS US study (protocol: 101468/249), patients were randomized (1:1) to receive ropinirole (0.25-4.0 mg/day, titrated as needed and tolerated) or placebo, once daily 1-3 hours before bedtime, for 12 weeks. Patients with ≥10 PLM/h (when supine throughout the night; PLM Index [PLMI]) at baseline (223/381 randomized) were included in analyses of the changes from baseline in PLMI, and in *post-hoc* analyses of the changes in IRLS total score and Sleep Problems Index II.

Results: At Week 6 observed case, improvements (reductions) in PLMI and IRLS total score were statistically significantly greater in ropinirole-treated patients compared with those receiving placebo: PLMI adjusted mean treatment difference (AMTD): -14.5 (95% CI: -20.3, -8.7; p<0.001); IRLS total score AMTD: -4.3 (95% CI: -6.3, -2.3; p<0.001). At Week 12 last observation carried forward, improvements in IRLS total score were again statistically significantly greater in the ropinirole group, compared with placebo (AMTD: -3.8: 95% CI: -6.0, -1.7; p<0.001), as were improvements in the MOS Sleep Scale Sleep Problems Index II (AMTD: -8.1; 95% CI: -12.7, -3.5; p<0.001).

Conclusions: Ropinirole was associated with concurrent improvements in objective motor and subjective RLS and sleep symptoms in RLS patients with PLM.

Study supported by: GlaxoSmithKline R&D.

References:

1. Allen RP et al. Sleep Med 2003; 4: 101'19.

2. Montplaisir J et al. Mov Disord 1997; 12: 61'65.

NR847 Wednesday, May 24, 3:00 PM - 5:00 PM

Responder/Numbers-Needed-to-Treat Analysis of Acamprosate in Alcohol Dependence in the Context of Current CNS Therapy

Khalil Saikali, Ph.D. *Forest Laboratories, Inc., Harborside Financial Center, Plaza V, Jersey City, NJ, 07311*, James Perhach, Ph.D., Daozhi Zhang, Ph.D., Allyson Gage, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to examine the efficacy of acamprosate across pivotal trials using various definitions of response in the context of other CNS pharmacotherapies.

Summary:

Introduction: Despite the availability of pharmacologic options for the treatment of alcohol dependence, the use of such agents is not as prevalent compared with drugs used for treating other CNS disorders. Multiple controlled clinical trials have demonstrated the efficacy and safety of acamprosate for the maintenance of abstinence in alcohol-dependent patients. This analysis examines efficacy data across three pivotal trials using various clinically relevant response definitions.

Methods: Intent-to-treat (ITT) data from three double-blind, placebo-controlled trials were retrospectively pooled to examine the proportion of patients who responded to acamprosate (1998 mg/day) or placebo using different responder definitions. Numbers-needed-to-treat (NNT) analyses were completed for each definition.

Results: In the ITT population (acamprosate, n=372; placebo, n= 375), the percentage of acamprosate responders was significantly greater than placebo for each response definition: patients abstinent at two thirds or more study visits (45% versus 28%, respectively; $p<0.0001$); patients with percent days abstinent (PDA) ≥90 (41% versus 22%; $p<0.0001$); and patients with PDA ≥90 and Clinical Global Impression of Improvement scores of 1 (very much improved) or 2 (much improved) (36% versus 15%; $p<0.0001$). NNT for achieving good response was between 5 and 6.

Conclusions/Discussion: Acamprosate effectively maintains abstinence in alcohol-dependent patients; the magnitude of treatment effect is comparable to other CNS therapies.

References:

1. Paille FM, Guelfi JD, Perkins AC, Royer RJ, Steru L, Parot P: Double-blind randomized multicentre trial of acamprosate in maintaining abstinence from alcohol. Alcohol Alcohol 1995; 30:239-247.
2. Sass H, Soyka M, Mann K, Zeiglgansberger W: Relapse prevention by acamprosate. Results from a placebo-controlled study on alcohol dependence. Arch Gen Psychiatry 1996; 53:673-680.

NR848 Wednesday, May 24, 3:00 PM - 5:00 PM

Genetic Polymorphism of BDNF and Psychopathological Correlates of Suicidal Behaviour

Marco Sarchiapone *University of Molise, Department of Health Sciences, Via De Sanctis, Campobasso, 86100, Italy*, Vladimir Carli, M.D., Chiara Cuomo, M.D., Alessandra Babore, M.Psy., Alec Roy, M.D.

Educational Objectives:

At the conclusion of this presentation, tha participant should be informed about new research findings on psychopathology and genetics of suicidal behavior.

Summary:

Background: Mounting evidence has documented a genetic susceptibility to violent behaviours, including suicide, and associations were found between suicidal behaviours and 5HT genes plymorphisms. Post-mortem studies have also reported a reduced BDNF expression in brain samples of completed suicides. Our study aimed at investigating putative associations between BDNF genetic polymorphisms and suicidal behaviours, with its psychopathological correlates such as impulsivity, aggressiveness, severity of depression, low resiliency, and childhood trauma.

Method: 156 suicide attempters were consecutively recruited from Univeristy Hospital "A.Gemelli" of Rome. Diagnosis was unipolar depression. Patients were assessed with the following psychometric scales: HDRS, BGHAI, CTQ, CD-RISC to evaluate underlying psychopatological features.

Results: We calculated the ratios for wild gene, heterozygosis and homozygosis for the Val66Met mutation of BDNF gene. No statistically significant differences were found between suicide attempters and controls for correlations to suicidal behaviour per se and its psychopathological variables.

Conclusion: Our results are inconsistent with previous reports of an involvement of BDNF in suicidal behaviours; discrepancy could be due to the low magnitude of our sample and sampling biases.

References:

1. Dwivedi Y, Rizavi HS, Conley RR, Roberts RC, Tamminga CA, Pandey GN. Altered gene expression of brain-derived neurotrophic factor and receptor tyrosine kinase B in postmortem brain of suicide subjects. Arch Gen Psychiatry. 2003 Aug;60(8):804-15.
2. Karege F, Vaudan G, Schwald M, Perroud N, La Harpe R: Neurotrophin levels in postmortem brains of suicide victims and the effects of antemortem diagnosis and psychotropic drugs. Brain Res Mol Brain Res. 2005 May 20;136(1-2):29-37.

NR849 Wednesday, May 24, 3:00 PM - 5:00 PM

Acamprosate Decreases the Severity and Duration of Relapse and Aids in Post-Relapse Recovery of Abstinence in Alcohol-Dependent Patients

Eugene Schneider, M.D. *Forest Laboratories, Inc., Harborside Financial Center, Plaza V, Jersey City, NJ, 07311*, Khalil Saikali, Ph.D., Daozhi Zhang, Ph.D., Allyson Gage, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the efficacy of acamprosate in reducing relapse severity in alcohol-dependent individuals who return to drinking, as measured by quantity/frequency of alcohol consumption and duration of relapse episodes, and acknowledge the value of continuing acamprosate therapy in the event of a relapse.

Summary:

Introduction: A major goal of alcohol-dependence treatment is relapse prevention. Acamprosate, with psychosocial support, is effective in helping alcohol-dependent patients maintain abstinence and, following relapse, regain abstinence. In the current analysis, we examined the effect of acamprosate on the severity of relapse in patients who returned to drinking, and assessed their post-relapse recovery.

Methods: The intent-to-treat (ITT) population from three double-blind, placebo-controlled, multicenter, pivotal trials (13-, 48-, and 52-weeks) receiving acamprosate 1998 mg/day (n=372) or placebo (n=375), in combination with psychosocial therapy, were evaluated on the quantity of alcohol consumption during relapse (at Day 0, 30, 60, 90, and last visit). Weekly frequency of alcohol consumption (13-week study) and duration of individual relapse episodes (48-week study) were also reported. In an ITT population subset with ≥1 documented relapse before last study visit, the rate of complete abstinence, percent days abstinent, and time to first drink were analyzed on abstinence periods following a relapse.

Results: Of 747 patients, 616 relapsed over the course of the studies (placebo, 89%; acamprosate, 76%). Post-relapse recovery was evaluated in patients who relapsed before the last study visit (n=587). Pooled data showed that a significantly smaller proportion of acamprosate- than placebo-treated patients reported consuming >5 standard drinks per day during the interval preceding Day 30, 60, 90 and last study visit ($p<0.01$). Acamprosate was statistically superior to placebo ($p<0.05$) with respect to frequency of alcohol consumption during relapse (13-week study) and for relapse duration (48-week study). A significantly greater propor-

tion of patients treated with acamprosate than placebo regained abstinence following initial relapse and maintained it for the remainder of the trial (13% versus 5%, respectively; p<0.001).

Conclusions/Discussion: In addition to helping alcohol-dependent patients maintain abstinence, acamprosate reduces relapse severity in patients who return to drinking and aids in abstinence recovery.

References:

1. Pelc I, Verbanck P, Le Bon O, Gavrilovic M, Lion K, Lehert P: Efficacy and safety of acamprosate in the treatment of detoxified alcohol-dependent patients. A 90-day placebo-controlled dose-finding study. Br J Psychiatry 1997; 171:73-77.
2. Sass H, Soyka M, Mann K, Zieglgansberger W: Relapse prevention by acamprosate. Results from a placebo-controlled study on alcohol dependence. Arch Gen Psychiatry 1996; 53:673-680.

NR850 Wednesday, May 24, 3:00 PM - 5:00 PM

Ropinirole Reduces Severity of Restless Legs Syndrome Symptoms

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Educational Objectives:

At the conclusion of this session, the participant should be able to understand the effect of ropinirole, a dopamine agonist, on the severity of Restless Legs Syndrome (RLS), as measured by the Clinical Global Impression-Severity of Illness scale and relevant items from the International Restless Legs Scale.

Summary:

Introduction: The effect of ropinirole on severity of RLS symptoms was examined using global and disease-specific assessments.

Methods: In three 12-week, double-blind studies (TREAT RLS 1, 2, and US), patients with moderate-to-severe primary RLS were randomized (1:1) to placebo (n=469) or ropinirole (n=465), 0.25-4.0mg once daily, titrated as needed and tolerated. The proportion of patients classified as normal/not at all ill (1) or borderline ill (2) on the Clinical Global Impression-Severity of Illness (CGI-S) scale (1-7) was analyzed *post hoc*, as were patient responses to International Restless Legs Scale (IRLS) Items 6 (severity of RLS as a whole) and 8 (average severity of symptoms judged by duration per day), each rated on a scale from "none" to "very severe" (0-4).

Results: At Week 1 (observed case), significantly more patients receiving ropinirole (21%) than placebo (8%) were classified as normal or borderline ill on the CGI-S scale (odds ratio [OR]=3.4; 95%CI: 2.2, 5.1; p<0.001). This treatment effect was maintained through Week 12 (last observation carried forward): 45% versus 33%; OR=1.7; 95%CI: 1.3, 2.2; p<0.001. In addition, among patients with at least moderate responses on IRLS Item 6 and/or 8 at baseline, a statistically significant difference in favor of ropinirole versus placebo was shown at Week 12 (p<0.001 for each of these IRLS items); a greater proportion of ropinirole-treated patients reported an overall RLS severity of "none" or "mild", compared with placebo (64% versus 48%). The same was true for the proportion reporting an average RLS symptom severity as judged by duration per day of "none" or "mild" (51% versus 40%).

Conclusions: Ropinirole treatment for RLS reduced severity of illness as measured both by a global measure and by disease-specific measures (overall symptom severity and symptom severity in terms of duration).

Study Supported By: GlaxoSmithKline Research & Development.

References:

1. Allen R et al. Sleep Med 2003; 4: 101'19.
2. Littner MR et al. Sleep 2004; 27: 557'9.

NR851 Wednesday, May 24, 3:00 PM - 5:00 PM

Industry Support for Psychiatric Research

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Educational Objectives:

Recognize the influence of pharmaceutical industry on psychiatric research

Summary:

The pharmaceutical industry has become a major source of funding for medical research. This has led to speculation and suggestion that there is a pro-industry bias in such "industrialized" research. The American Psychiatric Association (APA), along with many other national and international scientific organizations has adopted a policy of public disclosure of any relationship between the industry sponsorship and authorship. To study the impact of this policy, all abstracts (N=889) of the New Research presented/published at the 158th annual meeting of the APA were reviewed. There were 292 abstracts (32.85%) which appeared to have some relationship with the industry. Out of these abstracts, there were 225 (77.05%) abstracts which were clearly labeled as "Supported by Industry" as required by policy of the APA. The rest of the abstracts (N=67, 22.95%) were first-authored by an employee of the industry. It was also noted that 40 of the 225 "Supported by Industry" abstracts were also first-authored by an employee of the industry. That is, 107 abstracts (36.65%) were first-authored by an employee of the industry. It was interesting to note that there were 62 (21.23%) abstracts studying non-pharmaceutical subjects. In 194 abstracts (66.44%), the outcome favored the study drug in contrast to only 6 abstracts (2.05%) showing the study drug to be inferior, and 30 abstracts (10.28%) showing the study drug to be no better or worse (P<0.005). These observations do suggest that the industry has a significant financial impact upon psychiatric research. There is a tendency to report positive or favorable outcome for a particular study drug. This shows that the APA's policy does work in making the potential of pro-industry bias as transparent as possible in "Supported by Industry" abstracts. But the policy falls short on evaluating for such bias on abstracts first-authored by an employee of the industry.

References:

1. Perlis RH, Perlis CS, Wu Y et al : Industry sponsorship and financial conflict of interest in the reporting of clinical trials in psychiatry. Am J Psychiatry 2005;162:1957-60.
2. Buchkowsky SS, Jewesson PJ : Industry sponsorship and authorship of clinical trials over 20 years. Ann Pharmacother. 2004:38:579-85.

NR852 Wednesday, May 24, 3:00 PM - 5:00 PM

Diagnostic Issues and Comorbidity Patterns in Women Referred for Postpartum Depression

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Educational Objectives:

At the conclusion of this presentation, the participants should have developed an understanding of the diagnostic profile of women with postpartum depression.

Summary:

Objective: To investigate the diagnostic breakdown of women referred for postpartum depression.

Methods: Thirty-eight women seen consecutively with the referral diagnosis of postpartum depression were interviewed using structured instruments to gather information regarding DSM-IV Axis I diagnoses.

Results: In terms of frequency of occurrence, the primary diagnoses in this sample were: bipolar II disorder (34%), bipolar I disorder (24%), MDD (24%), and bipolar disorder NOS (18%). A currently comorbid disorder, with no lifetime comorbidity, occurred among 26% of the sample; by contrast, a lifetime comorbidity alone (i.e., with no currently comorbid disorder) was found among 32%. Both a lifetime and a current comorbidity was found among 13% of the women, and 29% had no comorbid disorder. The most frequently occurring current comorbid disorder was an anxiety disorder (86%). For lifetime comorbidity, substance use (42%) and anxiety (38%) disorders were the two most common.

Limitations: Small sample size.

Conclusions: The results suggest that postpartum depression is a heterogeneous entity and that misdiagnosis of bipolar disorders in the postpartum period may be quite common. The findings have important clinical implications including the need for early detection of bipolarity through the use of reliable and valid assessment instruments, and implementation of appropriate prevention and treatment strategies.

References:

1. Hunt N, Silverstone T: Does puerperal illness distinguish a subgroup of bipolar patients? J Affect Disord 1995; 34: 101-107.
2. Sharma V: Bipolar depression: the neglected realm of postpartum disorders. Curr Psych Rev 2005; 1: 325-329.

NR853 Wednesday, May 24, 3:00 PM - 5:00 PM

Exploring the Work Identities of People With Mental Illness Returning to Work

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Educational Objectives:

After this poster presentation, participants should be able to identify the dimensions of the seven work-identity profiles, the challenges for each profile group, and suggestions for the support and advocacy for people with different profiles. Participants should be particularly aware of the issues for people who are Foreclosed and Foreclosed/Diffused.

Summary:

Objective

Benefits of meaningful work are documented in the research literature, yet many people with mental illness are unemployed. While supported employment programs have demonstrated success in gaining work experiences for people with mental illness, we assert that recovery-focused, identity-centred approaches will address specific challenges that are confronted upon return to work.

Results will be presented from an exploratory study of work identity among people with mental illness who are returning to work. Implications of the findings will be discussed in relation to clinical practice and advocacy. Individuals with Foreclosed and Foreclosed/Diffused identities may be challenging for counselors and will be discussed in more detail.

Method

Maximum variation sampling (Patton, 1990) was used to recruit 14 participants from an employment program. All completed the study. Main criteria for inclusion were a DSM IV diagnosis of mental illness and an expressed interest/involvement in work.

Participants were interviewed using a semi-structured interview that was developed with input from people with mental illness. Qualitative data were analyzed according to the tenets of grounded theory technique (Lincoln and Guba, 1985).

Results

Seven work identity profiles emerged from the data. Individuals were assigned identities according to their work commitment, approach/avoidance, and anxiety. Factors accounting for assignment to each profile were also identified. Foreclosed and Foreclosed/Diffused individuals were older workers who felt that their only options were to return to their previous work settings.

Conclusion

Work identity profiles will enable counselors to use different strategies for supporting people in returning to work. Foreclosed and Foreclosed/Diffused workers may benefit from strategies that help them to recognize the range of options available to them, and assess the challenges of returning to their previous workplace. Advocacy strategies with former employers will also assist in the return to work.

References:

1. Marcia JE: Identity in Adolescence. In Handbook of Adolescent Psychology, edited by Adelson J, New York, Wiley, 1980, pp 159-181.
2. Tschopp MK, Bishop M, Mulvihill M: Career development of individuals with psychiatric disabilities ' an ecological perspective of barriers and interventions. Journal of Applied Rehabilitation Counseling 2001; 32:25-30.

NR854 Wednesday, May 24, 3:00 PM - 5:00 PM

A Study on Depressive Symptoms of Married Women in Korean Urban Area

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Educational Objectives:

This study was conducted for mental health of married women in Korean urban area. We surveyed 123 married women, and they consisted of the groups with job and without job. In results, this study demonstrated on the Psychosocial Factors Associated with Depressive Symptoms of Married Women in Korean Urban Area

Summary:

Introduction : This study examined relationship between depressive symptoms and psychosocial factors including the state of employment, self-esteem and social support in 123 married women in Korean urban area.

Methods : Among the subjects, 74 had jobs and 49 were not-employed, and they completed Beck Depression Inventory, Symptom Checklist-90-Revision, Self Esteem Scale, Social Support Scale and Achievement Self Esteem Scale. The demographic data and the scores of the each scales were compared in two groups. Descriptive statistics, t-test, χ^2-test and stepwise regression analysis were applied to analyze the data.

Results : There was no significant difference in the demographic data, and the scores of mental symptom scales and psy-

chosocial factor scales between two groups. Independent of the state of employment of the subject, degree of depressive symptoms was associated with the educational level of the woman and the income of her family. And depression was also related with low self-esteem and lack of social support.

Conclusion : Our findings suggest that we need to consider the psychosocial factors of an individual patient such as the educational level and family finances, and the degree of self-esteem and social support of a married woman, when evaluating her mental health status.

References:

1. Bebbington PE : The origins of sex difference in depressive disorder: bridging the gap. Int Rev Psychiatry 1996; 8 : 295-332.
2. Krause N, Geyer-Pestello HF: Depressive symptoms among women employed outside the home. Am J Comm Psychol 1985; 13 : 49-67.

NR855 Wednesday, May 24, 3:00 PM - 5:00 PM

Hepatic Safety of Once-Monthly, Long-Acting Intramuscular Naltrexone (LA-NTX) in Alcohol-Dependent Subjects: A Pooled Analysis From Two Clinical Studies

Bernard Silverman *Alkermes, 88 Sidney Street, Cambridge, MA, 02139,* Michael Lucey, Ari Illeperuma, Charles P. O'Brien

Educational Objectives:

At the conclusion of this session participants should better understand the hepatic safety profiles of LA-NTX and oral naltrexone (NTX).

Summary:

Background: Oral NTX is an effective agent for the treatment of alcohol dependence. LA-NTX, which is administered IM once monthly, provides continuous one-month exposure to NTX. It may improve compliance as compared with daily oral NTX, while also reducing total monthly naltrexone dose and avoiding first-pass hepatic metabolism.

Objectives: To assess the hepatic safety profile of monthly injections of LA-NTX in alcohol-dependent subjects following 6 months of treatment.

Methods: Safety data were pooled from 2 studies: 1) a 6-month efficacy study that included 414 alcohol-dependent subjects who received LA-NTX 380 mg (n=205) or placebo (n=209); and 2) the first 6 months of a 1-year safety study that included 371 patients on LA-NTX 380 mg and 65 patients on oral NTX 50 mg/day. The second study also included 121 patients with opioid or mixed alcohol-opioid-dependence. Serum AST, ALT, GGT, and bilirubin were measured every 4 weeks.

Results: The mean±SD values for ALT and AST at baseline and 6 months showed no significant group differences. For each group, baseline versus 24-week ALT values (U/L) were: placebo, 34.0±21.8 versus 31.9±22.1; oral NTX, 27.9±20.3 versus 27.4±14.4; LA-NTX 380 mg, 31.4±20.5 versus 28.9±23.4. Baseline and 24-week AST values (U/L) were: placebo, 31.9±18.1 versus 30.5±19.1; oral NTX, 26.9±15.3 versus 28.7±19.5; LA-NTX 380 mg, 29.0±14.8 versus 28.4±20.6.

The proportions of subjects with normal ALT and AST increased slightly from baseline in all groups. GGT decreased over the 24-week study period, more with LA-NTX 380 mg versus placebo, which is consistent with reduced drinking. No changes in bilirubin were observed across groups.

Conclusion: In alcohol-dependent subjects, the 6-month hepatic safety profile of LA-NTX is similar to that of placebo.

References:

1. Grant BF, Dawson DA, Stinson FS, Chou SP, Dufour MC, Pickering RP. The 12-month prevalence and trends in DSM-IV alcohol abuse and dependence: United States, 1991-1992 and 2001-2002, Drug Alcohol Depend 2004;74;223-34.
2. Garbutt JC, Kranzler HR, O'Malley SS, et al. Vivitrex Study Group. Efficacy and tolerability of long-acting injectable naltrexone for alcohol dependence: a randomized controlled trial. JAMA 2005;293;1617-25.

NR856 Wednesday, May 24, 3:00 PM - 5:00 PM

Transmucosal Zolpidem: Pharmacokinetic and Pharmacodynamic Profile Supports Middle-of-the-Night Dosing

Meeta Singh, M.D. *Henry Ford Hospital, Sleep Medicine, 2799 West Grand BLVD., CFP 3, Sleep Centre, Detroit, MI, 48902,* Bruce C. Corser, M.D., Nik singh, Ph.D., Barbara Roth-Schechter, Ph.D., Adam Roth, M.D., I. Pather, Pharm.D., Thomas Roth, Ph.D.

Educational Objectives:

To test if middle of the night awakenings, in insomniacs,can be treated prn with a sleeping aid with a rapid onset of action and a short duration of action.

Summary:

Introduction: Middle-of-the-night (MOTN) awakenings in insomniacs are not currently treated prn. TMZ, with rapid onset and short duration of action could be useful in treating MOTN insomnia.

Methods: Healthy adults (n=24, mean age=37.6 yrs) were tested in this double-blind, placebo-controlled, 4-way crossover study of 2 consecutive days with morning dosing with placebo, 1, 1.75 or 3.5 mg TOZ. On day 1 of each period, PD endpoints were evaluated at pre-dose, and at 20 minutes, 1, 1.5, 2, 3, 4, and 5 hours post-dose. On day 2, repeated blood samples were drawn for PK analysis over 12 hours.

Results: TMZ Cmax (maximum drug concentration) and AUC (area under the plasma concentration curve) were dose-proportional: Tmax (time at which Cmax occurs) was 36.0, 37.9, and 37.9 minutes for 1.0, 1.75, and 3.5 mg of TMZ. TMZ plasma levels higher than 20 ng/mg occurred between 15 and 240 minutes. Significant reductions in Digit symbol substitution test (DSST) occurred after 1.75 and 3.5 mg TMZ as early as 20 minutes (-6.6; p=0.0132, and -14.5;p<0.001) and lasted for 1.5 hours post-dose. Other PD outcomes exhibited similar profiles.

Conclusions: At a dose and a Tmax of less than half of the approved dose of zolpidem (ambien©) (10 mg) in adults, TMZ demonstrates potential for faster sleep onset with prn administration for MOTN insomnia

References:

1. Mendelson WB: Human Sleep: Research and Clinical Care. New York, Plenum Press, 1987.
2. Langtry HD, Benfield P: Zolpidem: A review of its pharmacolodynamic and pharmacokinetic properties and therapeutic potential. Drugs 1990; 40: 291-313.

NR857 Wednesday, May 24, 3:00 PM - 5:00 PM

Eszopiclone Treatment During Menopausal Transition: Sleep Effects, Impact on Menopausal Symptoms,and Mood

Claudio N. Soares, M.D. *Mass General Hosp. Center for Women's Health, 15 Parkman Street, WAC 812, Boston, MA, 02114,* Hadine Joffe, M.D., Robert Rubens, M.D., David A. Amato, Ph.D., James M. Roach, M.D., Judith Caron, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to evaluate the effect of eszopiclone 3 mg on (1) the treatment of insomnia associated with menopausal transition, and (2) changes in mood, menopause-related symptoms, and quality of life.

Summary:

Objective: This study evaluated 1) eszopiclone 3mg in the treatment of insomnia associated with menopausal transition, and 2) the impact of treating insomnia on changes in mood, menopause-related symptoms, and quality of life (QOL).

Methods: This double-blind, placebo-controlled study included 410 women meeting menopause STRAW criteria stages -2, -1, or 1a (a peri-menopausal population), who reported sleep latency (SL) ≥30 minutes and total sleep time (TST) ≤6 hours/night. Patients received eszopiclone or placebo nightly for 4 weeks. Sleep endpoints were reported daily. Physician global evaluations of menopause (PGE), menopause-specific QOL questionnaire (MenQOL), Greene Climacteric Scale (GCS), the Montgomery Asberg Depression Rating Scale (MADRS), and the Sheehan Disability Scale (SDS) were collected at baseline and end of treatment.

Results: Patients receiving eszopiclone reported significantly greater improvements in SL, sleep maintenance (awakenings and time awake after sleep onset), TST, sleep quality (all p-values<0.0001 versus placebo), and awakenings due to hot flushes (p=0.001). No differences in the number or severity of daytime hot flushes were found. Patients treated with eszopiclone had significantly greater improvements in MADRS scores (p<0.03) and PGEs (p<0.0001) compared with patients treated with placebo; total GCS score (baseline scores were 14.8 in each group; change scores were -2.18 for placebo and -3.57 for eszopiclone) and the vasomotor and psychological subscales (p<0.05 versus placebo); vasomotor and physical domains of the MenQOL (p<0.05); and family life/home disability domain using the SDS (p<0.05). The most common adverse event was unpleasant taste in those receiving eszopiclone (18.1% versus 0.5%). Other adverse events (ie, headache, pain) were similar in the two groups.

Conclusion: In this study, eszopiclone produced significant improvements in sleep and positively affected mood, QOL, and menopause-related symptoms in peri-menopausal women.

Support for this study provided by Sepracor Inc.

References:

1. Krystal AD, Walsh JK, Laska E, Caron J, Amato DA, Wessel TC, Roth T: Sustained efficacy of eszopiclone over 6 months of nightly treatment: results of a randomized, double-blind, placebo-controlled study in adults with chronic insomnia. Sleep 2003;.

2. Zammit GK, McNabb LJ, Caron J, Amato DA, Roth T: Efficacy and safety of eszopiclone across 6-weeks of treatment for primary insomnia. Current Medical Research and Opinion 2004; 20(12):1979-1991.

NR858 Wednesday, May 24, 3:00 PM - 5:00 PM

Air Pollution and Suicide

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Educational Objectives:

To recognize that air pollutants might be associated with suicide, potentially via activation of cytokines.

Summary:

Introduction: Certain cytokines exacerbate depression and may precipitate suicide[1]. We hypothesized that air pollutants, via nonspecific cytokine release, could lead to an increased incidence of suicide in vulnerable individuals. Therefore, we expected to find a positive association between pollution and suicide rates.

Methods: We analyzed suicide rates and the air pollutants CO, SO_2, O_3, NO_2, Pb, PM2.5, and PM10 between 1999 and 2002 in 193 US counties. Data sets were obtained on suicide (National Center for Health Statistics mortality database), air pollution (Environmental Protection Agency), and county population (US Census Bureau). Preliminary analysis examined the association between four year averages in county suicide rates and pollutants, while adjusting for regional and county population covariates, using a multiple linear regression model.

Results: US region (West, South, Midwest, Northeast; p<0.001), county population size (p<0.001), and SO_2 concentration (p<0.005) explained 36.6% of the variance in county suicide rates; other relationships were not significant. Analysis of additional covariates and potential confounders is in progress.

Conclusions: This is, to our knowledge, the first reported relationship between air pollution and suicide. Limitations inherent to ecologic models acknowledged, a link between SO_2 exposure and suicide is consistent with previously described associations between suicide and chronic respiratory disease[1], which is exacerbated by SO_2, an air pollutant known to induce cytokine release in the respiratory tract.[2]

References:

1. Postolache TT, Komarow HD, Stiller JW, and Tonelli T. 2005. Allergy, Depression, and Suicide. Directions in Psychiatry 25(1):59-70.

2. Koksal N, Yildirim Z, Gokirmak M, Hasanoglu HC, Mehmet N, and Avci H. 2003.. The role of nitric oxide and cytokines in asthma-like syndrome induced by sulfur dioxide exposure in agricultural environment. Clinica Chimica Acta 335:115-122.

NR859 Wednesday, May 24, 3:00 PM - 5:00 PM

Warmth Detection: An Alternative Sensory Assessment in Opiate Abuse

Matthew Steinfeld *Beth Israel Medical Center, 1st Avenue and 16th Street - 6Karpas, New York, NY, 10003*, Steven Frenda, Lisa J. Cohen, Ph.D., James Prosser, M.D., Igor I. Galynker, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize hypoalgesia may be associated with protracted opiate abstinence, and that warmth detection administered via sensory analyzer is a particularly good method of assessing sensory abnormalities in this population.

Summary:

Abstract

Objective: Abnormal pain processing in opiate abusers may contribute to the perpetuation of addictive behaviors. Painful heat is frequently used to assess pain processing, but there are difficulties studying pain perception in former opiate abusers. Because of their higher pain thresholds, there is the potential to cause tissue damage at the temperatures needed to register a painful stimulus. Warmth detection, which is mediated by similar neural pathways as painful heat, may be abnormal in opiate addicts as well, and be an alternative method of assessing atypical sensitivity. This study examines warmth detection in former opiate abusers and non-drug using controls.

Methods: Forty-six subjects, 14 male and 9 female former opiate addicts in protracted- abstinence (PA), and 13 male and 10

female Controls (C) between the ages of 21 and 60 were recruited for study. Subjects were run through a sensory assessment battery on the TSA-II Neuro-Sensory Analyzer © to assess pain and warmth thresholds. PA subjects were a minimum of six months drug-free.

Results: There was no significant difference between groups on pain threshold detection. A significant difference was observed between PA and Control subjects on warmth detection ($F(1,44) = 8.26$, $p = .006$). When males and females were analyzed separately, significant differences across groups were only found in males ($t(16.2) = 2.86$, $p=.011$).

Conclusion: Warmth detection was found to be abnormal in detoxified former male opiate abusers. Warmth detection may be a useful, non-noxious, alternative to pain-threshold detection in studying abnormalities in pain / warmth processing following prolonged opiate misuse.

References:

1. Compton P, Charuvastratra VC, Ling W (2001) Pain intolerance in opioid-maintained former opiate addicts: effect of long-acting maintenance agent. Drug and Alcohol Dependence. 63, 139-146.
2. Liebmann PM, Lehofer M, Schonauer-Cejpek M. (1994) Pain sensitivity in former opioid addicts, Lancet, 344, 1031-1032.

NR860 Wednesday, May 24, 3:00 PM - 5:00 PM

Lamotrigine in Human Breast Milk and Nursing Infants

Zachary N. Stowe, M.D. *Emory University School of Medicine, 1635 Clifton Road, NE Suite# 6100, Atlanta, GA, 30322*, D. Jeffrey Newport, M.D., James Ritchie, Ph.D., Michael J. Owens, Ph.D., Melanee Newman, R.N., Jean Montgomery, R.N., Page B. Pennell, M.D.

Educational Objectives:

At the conclusion of this presentation, attendees will be familiar with the excretion of anti-epileptic drugs into breast milk and nursing infant exposure to lamotrigine.

Summary:

The efficacy of the anti-epileptic, lamotrigine (LTG), in treating women with epilepsy and bipolar disorder underscores the need to more clearly define the reproductive safety issues of using LTG both in pregnancy and lactation. The current study employed the methodology of our previous investigations (Stowe et al 2001) to determine nursing infant exposure and provide options for decreasing infant exposure.

A total of 12 women who chose to breast feed while being treated with lamotrigine were included in the present study. Women were instructed in two breast milk collection procedures- Gradient (from fore milk to hind milk) using 10 ml aliquots and Time Course, collecting the first 10 ml of breast milk at 4 hour intervals over a 24 hour period. A total of 123 breast milk samples were collected and assayed blind to maternal daily dose.

The concentration of LTG in breast milk was highly variable (<0.5-18.1 μg/ml). The milk / plasma ratio which ranged from 0.18-0.80 (0.49±0.2) is consistent with several previous investigations of AEDs. Presently, complete data sets were only available from 8 women as mathematical modeling failed to identify a significant equation for both the gradient and time course. There was a trend to see higher concentrations of LTG at 4-6 hours post dose, and a bimodal peak in fore milk and hind milk. Using the available data the estimated infant dose ranged from 0.86 to 6.94 mg/day. Nursing infant sera concentrations (n=7) were typically at the limits of detection. No adverse effects were observed.

The impact of infant dose on infant serum concentration will be discussed, as well as the potential to reduce nursing infant exposure using both dosing and "pump and dump" strategies.

Supported by P50 MH 68036 and R01 MH-71531

References:

1. Stowe ZN, Hostetter A, Owens MJ, Ritchie JC, Sternberg K, Cohen LS, Nemeroff CB: Pharmacokinetics of sertraline excretion into human breast mik: determinants of infant serum concentrations. J Clinical Psychiatry 2003; 64(1):73-80.
2. Ragan K, Stowe ZN, Newport DJ: The use of antidepressants and mood stabilizers in breast feeding women. In Mood and Anxiety Disorders during Pregnancy and Postpartum, edited by Cohen LS, Nonacs RM, Washington DC, Am. Psy. Pub., 2005, pp105-144.

NR861 Wednesday, May 24, 3:00 PM - 5:00 PM

A Transportable PTSD Intervention Shows Promise for Women Veterans With Military Sexual Trauma

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to:

1. Understand the incidence and sequelae of military sexual trauma.
2. Describe a treatment model for posttraumatic stress disorder that incorporates guided imagery techniques in a transportable, patient-directed format
3. Discuss the results of a feasibility pilot of a transportable, patient-directed intervention for posttraumatic stress disorder in women veterans with military sexual trauma.

Summary:

Objective: The deleterious effects of sexual trauma are well established, and include high rates of posttraumatic stress disorder (PTSD), depression, substance abuse, and health service use. Over 50,000 veterans have been identified as having experienced military sexual trauma (MST). This number is likely to further increase as currently deployed troops return and access VA services. Because current MST treatments are intensive, costly, and highly specialized, access to these services remains limited. The high volume of MST cases necessitates the development of transportable, scalable interventions that can be rapidly disseminated. To address this challenge, we developed a novel MST intervention called GIFT: Guided Imagery For Trauma.

Method: We conducted a trial of the 12-week GIFT intervention in 14 women veterans with MST-related PTSD, recruited from the Durham VAMC. PTSD symptoms were screened with the PTSD Checklist (PCL) and clinical diagnosis was confirmed with the Clinician Administered PTSD Scale (CAPS). The GIFT intervention includes audio-recorded exercises which patients complete independently, with collaborative guidance from a clinical facilitator. Contacts with the facilitator are scheduled to provide patient support and direction, and include 2 face-to-face sessions and 8 brief telephone calls.

Results: Of the initial sample of 14, 11 women completed the full study. Using repeated measures ANOVA, we found a large effect on PTSD symptoms, as assessed with the CAPS: Cohen's $d = .88$; $F(1,10) = 5.77$, $p = .04$. For PCL scores, Cohen's $d = 1.99$; $F(1,10) = 8.45$, $p = .01$.

Conclusion: Our pilot data demonstrate that GIFT reduces PTSD symptoms in a MST cohort, and that the self-directed format

can be feasibly administered and is well-tolerated by women veterans with MST. The treatment effects found in this pilot study are comparable to those reported for evidence-based psychotherapies for PTSD and well-above what would be expected for placebo alone.

References:

1. Fontana A, Rosenheck RA: Duty-related and sexual stress in the etiology of PTSD among women veterans who seek treatment. Psychiatr Serv 1998; 49:658-662.
2. Sadler AG, Booth BM, Cook BL, Doebbeling BN. Factors associated with women's risk of rape in the military environment. Am J Ind Med 2003; 43:262-273.

NR862 Wednesday, May 24, 3:00 PM - 5:00 PM

Treatment Patterns, Antipsychotic Drug Utilization, and Resource Consumption Among Short-Term Hospitalized Schizophrenia Patients in the U.S.

David Strutton, Ph.D. *Wyeth Research, Global Health Health Outcomes Assessment, 500 Arcola Road, Collegeville, PA, 19426*, Benjamin Gutierrez, Ph.D., Christopher Blanchette, M.A.

Educational Objectives:

Participants will gain a better understanding of antipsychotic medication management among hospitalized schizophrenia patients and the impact of medication selection, dose changes, and concomitant medications on resource consumption.

Summary:

Objective: This study investigates treatment patterns, antipsychotic drug utilization, and resource consumption among short-term hospitalized schizophrenia patients in the US.

Methods: Patients hospitalized with a primary diagnosis of schizophrenia (295.xx) discharged between October 1, 2003 and September 30, 2004 were identified from a large administrative multi-hospital database. The duration of dose adjustment was defined as the period between first and last days of dose change. Ordinary least squares regression was utilized to examine relationships between labeled length of titration, actual duration of dose adjustment, and hospitalization resource use; while controlling for covariates.

Results: The study sample consisted of 21,950 hospitalized schizophrenia patients representing 30,873 hospitalizations from 150 hospitals. The majority of patients were 18-44 years old (56.3%), had Medicare (46.6%) as their primary insurance, and were admitted through the emergency room (55.5%). Average length of stay was 10 days (median 7 days) and 30% had a mental health readmission within 1 year. Labeled length of titration (varies from 0 to 3 days) was not correlated with actual duration of dose adjustment ($r=0.05$, $p<0.0001$) or with longer hospital stays ($r=-0.03$, $p<0.0001$). Drug utilization factors affecting hospitalization resource use included medication changes (3.00, $p<0.0001$), dose changes (0.82, $p<0.0001$), use of short-acting IM antipsychotic (2.08, $p<0.0001$) and EPS (0.76, $p<0.0001$) medications.

Conclusion: Antipsychotic medication changes, dose changes, and use of short-acting IM antipsychotics have a significant impact on inpatient resource use, while longer labeled length of titration was not associated with longer hospital stays. In addition, labeled length of titration was not correlated with actual patterns of dose changes. The frequency and duration of dose changes highlights the challenge of treating short-term hospitalized schizophrenia patient with currently available antipsychotics.

References:

1. Lieberman JA, Stroup TS, McEvoy JP, et al: Effectiveness of Antipsychotic Drugs in Patients with Chronic Schizophrenia. NEJM 2005;353:1209-1223.
2. Edlinger M, Hausmann A, Kemmler G, et al:Trends in the pharmacological treatment of patients with schizophrenia over a 12 year observation period. Schizophrenia Research 2005; 77: 25-34.

NR863 Wednesday, May 24, 3:00 PM - 5:00 PM

Effects of Ropinirole on Mood in Restless Legs Syndrome

Karen Thomas, D.O. *Ohio State University, 1581 Dodd Drive, Colunbus, OH, 43210*, Philip M. Becker, M.D., Carolyn B. Watson, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to understand the effects of ropinirole treatment on mood disturbance (as assessed by Item 10 of the International Restless Legs Scale [IRLS]), and anxiety and depression (as assessed by the Hospital Anxiety and Depression Scale [HADS]) in patients with moderate-to-severe primary Restless Legs Syndrome (RLS).

Summary:

Introduction: RLS has been associated with mood disturbances, such as anxiety and depression.[1,2] This negative impact on mood may be a result of the chronic nature of RLS and associated sleep disturbance. Ropinirole, a dopamine agonist, is the only FDA-approved treatment for moderate-to-severe primary RLS. Mood was assessed during one pivotal trial, the TREAT RLS US study (protocol: 101468/249).

Methods: Patients with moderate-to-severe primary RLS and International Restless Legs Scale (IRLS) total score ≥15 received ropinirole, once daily, 1-3 hours before bedtime, 0.25-4.0 mg/day, titrated as needed and tolerated, or placebo for 12 weeks. Effects on mood were assessed using Hospital Anxiety and Depression Scale (HADS) Anxiety and Depression subscales among patients with normal (*post hoc*) (≤7) or abnormal (*a priori*) (≥8) HADS subscale scores at baseline and by response to IRLS Item 10 (severity of mood disturbance; *post hoc*).

Results: A statistically significant treatment difference was observed in favor of ropinirole for IRLS total score at Week 12 last observation carried forward (LOCF) (adjusted mean treatment difference [AMTD]: -3.7 (95% CI: -5.4, -2.0; $p<0.0001$). Similar findings were demonstrated for IRLS Item 10 ($p=0.014$). Among patients with abnormal baseline anxiety scores, those receiving ropinirole (n=62) had a statistically significant reduction in HADS-Anxiety score at 12 weeks (LOCF) compared with placebo (n=67) (AMTD: -1.2; 95% CI: -2.3, -0.1; $p=0.0385$). No statistically significant differences were seen between treatment groups among patients with abnormal baseline HADS-Depression scores, or among patients with normal baseline HADS scores.

Conclusions: Ropinirole improves the overall symptoms of RLS, including mood disturbance. In addition, RLS patients with increased anxiety may experience improvement in anxiety symptoms following ropinirole treatment.

Study Supported By: GlaxoSmithKline Research & Development.

References:

1. Ulfberg J, et al. Mov Disord 2001; 16: 1159'63.
2. Sevim S et al. J Neurol Neurosurg Psychiatry 2004; 75: 226'230.

NR864 Wednesday, May 24, 3:00 PM - 5:00 PM

Ropinirole Improves Restless Legs Syndrome Symptoms in Women

Karen Thomas, D.O. *Ohio State University, 1581 Dodd Drive, Colunbus, OH, 43210*, June M. Fry, M.D., Tanya Simuni, M.D., Nancy L. Earl, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to describe the demographic characteristics of women with moderate-to-severe primary Restless Legs Syndrome (RLS) in three 12-week, double-blind clinical trials. They should be able to understand the effects of ropinirole treatment on the symptoms of RLS in women, and in women who were taking concomitant hormone replacement therapy (HRT).

Summary:

Introduction: The prevalence of RLS is higher in women than men[1] and increases with age.[2] However, no studies have specifically examined the effect of RLS treatment in women.

Methods: In three 12-week, double-blind studies (protocols: 101468/190, 194, and 249), patients (n=933) with moderate-to-severe primary RLS were randomized (1:1) to once-daily placebo or ropinirole, 0.25-4.0mg/day titrated as needed and tolerated, 1-3 hours before bedtime. Analysis of pooled data (*post hoc*) assessed efficacy among women in the overall analysis population and those on a stable dose of HRT. Efficacy measures included International Restless Legs Scale (IRLS) total score and proportion of patients classified as responders (much/very much improved) on the Clinical Global Impression-Improvement (CGI-I) scale after 2-3 nights, and at Weeks 1-6, 8, and 12.

Results: Mean (SD) ages were 53.9 (11.4) years for the ropinirole group (n=273) and 54.8 (12.4) years for placebo (n=297); approximately half had a family history of RLS (55% and 50%), over one-third had received prior RLS treatment (42% and 44%), and about one-quarter were receiving HRT (28% and 24%). A statistically significant treatment difference was observed in favor of ropinirole at all visits on IRLS total score (e.g., Week 12 last observation carried forward [LOCF], adjusted mean difference: -3.0; 95%CI: -4.4,-1.6; $p<0.001$), and for the proportion of CGI-I responders at all visits (e.g., Week 12 LOCF, ropinirole=63%; placebo=48%; odds ratio=1.9; 95%CI: 1.3,2.7; $p<0.001$) except Day 2 ($p=0.066$). Statistically significant treatment differences in favor of ropinirole were seen on both scales among women receiving HRT, at most visits, including Week 12. The three most commonly reported adverse events were nausea, headache, and somnolence.

Conclusions: Ropinirole effectively relieved RLS symptoms in women, including those receiving HRT. The safety profile was consistent with dopamine agonist treatment.

Study Supported By: GlaxoSmithKline Research & Development.

References:

1. Berger K et al. Arch Intern Med 2004; 164: 196'202.

2. Allen RP et al. Arch Intern Med 2005; 165: 1286'1292.

NR865 Wednesday, May 24, 3:00 PM - 5:00 PM

Antipsychotic Utilization: A Six-State Medicaid Study

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Educational Objectives:

At the conclusion of this presentation, the participant will recognize the scope of antipsychotic utilization, beyond the indications of schizophrenia and bipolar disorder, across diffferent geographical Medicaid populations.

Summary:

Second-generation atypical antipsychotic drugs (SGA's) are indicated for schizophrenia and bipolar disorder. The study assessed the prevalence of mental health (MH) disorders treated with SGA's compared to Conventional antipsychotics and detailed their patterns of use. A retrospective cohort study using Medicaid claims data from California, Nebraska, Oregon, Tennessee, Utah, and Wyoming evaluated 64,411 patients who received an antipsychotic between 1998 and 2003. Analysis was stratified by index antipsychotic. ICD-9 codes were used to identify mental health diagnoses. Groups were compared using chi-square tests. Regardless of MH diagnosis 65% of patients were initiated on SGA's, 31% Conventionals, 3% multiple antipsychotics, and 1% clozapine. While 88% of schizophrenia patients received an antipsychotic (SGA: 44%, Conventionals: 36%, Multiple: 5%), the prevalence of schizophrenia and bipolar diagnoses among antipsychotic users was 34% and 16% respectively. Index mental health diagnosis varied by index drug: SGA (12% schizophrenia, 22% depression, 5% bipolar, other 42%); Conventional (24% schizophrenia, 17% depression, 4% bipolar, other 37%); and Multiple (40% schizophrenia,11% depression, 5% bipolar, other 30%) ($p<0.001$). These findings indicate antipsychotic drugs were used frequently in non-schizophrenic, non-bipolar patients, with SGA's used more broadly than Conventionals. Clinical effectiveness for other indications should be evaluated.

References:

1. Ganguly R, Kotzan JA, Miller LS, et al.: Prevalence, trends, and factors associated with antipsychotic polypharmacy among Medicaid-eligible schizophrenia patients, 1998-2000. J Clin Psychiatry 2004; 65:1377-1388.

2. Schumacher JE, Makela EH, Griffin HR: Multiple antipsychotic medication prescribing patterns. Ann Pharmacother 2003; 37:951-955.

NR866 Wednesday, May 24, 3:00 PM - 5:00 PM

Developmental Psychopathology in Young Adults With Substance-Related Disorder

Patricia J. van Wijngaarden-Cremers *Zwolse Poort GGz, Addicition Psychiatry, dr. van Thienenweg 8, Zwolle, NL 8025 AL, The Netherlands*, Chris Couwenbergh, Jr., M.S.C., Jildou Heerschop, Jr., M.S.C., Wim Van Den Brink, Rutger J. Van der Gaag, Sr., M.D.

Educational Objectives:

Having read this poster the participant should be aware of the diversity of developmental disorders present in young adults with substance abuse disorder and what this requires in terms of assessement and therapeutic approach.

Summary:

Objectives

Co-morbidity in young adults with Substance abuse disorders is more rule than exception. In general "externalizing" comorbidity in men is most prevalent. But in none justice clinical settings for addiction psychiatry: more women and individuals with developmental disorders seem present. These reports are mostly anecdotal. To ascertain this presumption a chartreview was performed.

Methods

209 charts of subsequent admittances in an addiction clinic were reviewed using a standardised form. Developmental history

was ascertained. Rimland Autism Questionnaire that was taken from the individuals themselves and from one of the parents or siblings or partner.

Results:

Interrater reliability on ten randomly drawn charts (Cohen's Kappa's .91) was very good).

Data from 198 charts could be computed in eleven cases there were too many missing data.

In 59,3% dual diagnoses were found 32,8% had externalizing disorders (18,2% ADHD). Surprisingly 41% of the "conduct disorder/antisocial personality disorder group appeared to be women. But the most remarkable finding was that 8 cases (4,71%) had a classification Autism Spectrum Disorder.

Though in merely all cases substance use/abuse was present from 15 years of age on, less than 6% of all individuals with internalizing disorders, only 15,2% of the individuals with ADHD, 33% of the autistic individuals and 41,4% of the individuals with "externalizing" disorders had been seen, assessed and treated in Mental Health facilities (who in most cases did not acknowledge the substance abuse problems at that stage).

Conclusion

Limitations due to retrospective chart study of clinical cases.

Internalizing disorders, developmental disorders (ADHD & Pervasive Development Disorder) are more prevalent than has emerged from mainly community based studies in Addiction Psychiatry.

The majority of young adults in treatment for dual-diagnosis conditions had a psychiatric diagnosis and started their substance abuse carrier in mid-adolescence but assessed adequately at that time.

References:

1. Compton WM, Thomas YF, Conway KP, Colliver JD. Developments in the epidemiology of drug use and drug use disoders Am J Psychiatry 2005 162(8) 1494-1502.
2. van Nimwegen L, de Haan L, van Beveren N, van den Brink W, Linszen D. Adolescence, schizophrenia and drug abuse: a window of vulnerability. Acta Psychiatr Scand Suppl. 2005;(427):35-42.

NR867 Wednesday, May 24, 3:00 PM - 5:00 PM

Sertraline: An Analysis of Suicide-Related Events in Placebo-Controlled Clinical Trials

Douglas Vanderburg, M.D. *Pfizer, US Medical, 235 E 42nd street, New York, NY, 10017*, Evan Batzar, Charlotte M.E. Kremer, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be more aware of the risks of suicidal thinking or behavior in sertraline treated patients versus those treated with placebo

Summary:

Suicide is an inherent risk in depression and anxiety disorders. The current analysis, pursuant to a search strategy specified by the FDA, identified all possibly suicide-related adverse events with sertraline, active comparators or placebo in Pfizer-sponsored placebo-controlled, short-term studies (up to 17 weeks, with at least 30 patients) in MDD and all other indications (non-MDD).

For both sets of studies, the search strategy specified by the FDA identified the suicide-related adverse events occurring during the double-blind phase of treatment for phase 2 through phase 4 studies from the start of randomization through 1 day after stopping double-blind treatment. The narratives prepared for each case were assessed and classified by two psychiatrists blinded to the subject's treatment using the adverse event classification system provided by the FDA.

A total of 75 (19 MDD and 56 non-MDD) studies with 13,345 patients were included in the analysis (sertraline, n=6,561; placebo, n=5,480; active controls, n=1,304). Possible suicide-related adverse events were identified in 12 MDD and 36 non-MDD studies. There was 1 completed suicide with placebo, 18 suicide attempts in 18 patients (6 with sertraline, 7 with placebo, 2 with clomipramine, 2 with imipramine and 1 with desipramine); 3 preparatory acts toward imminent suicidal behavior (1 with sertraline, 1 with placebo and 1 with imipramine); 37 events of suicidal ideation in 37 patients (13 with sertraline, 20 with placebo, 2 with clomipramine and 2 with imipramine) and 1 case of self-injurious behavior of unknown intent with sertraline.

These data, compiled in accordance with a FDA-specified search strategy, show no increased risk of suicidal thinking or behavior in sertraline-treated patients versus those treated with placebo.

References:

1. Khan A, Khan S, Kolts R, Brown WA. Suicide rates in clinical trials of SSRIs, other antidepressants, and placebo: analysis of FDA reports. Am J Psychiatry 2003; 160:790-792.
2. Storosum JG, van Zwieten BJ, van den Brink W, Gersons BP, Broekmans AW.

NR868 Wednesday, May 24, 3:00 PM - 5:00 PM

Prevalence of Depressive and Anxiety Disorders in a Menopause University Outpatient Clinic

André B. Veras, Sr., M.D. *UFRJ/IPUB, Psychiatry, Rua Pereira da Silva 172,201, Laranjeiras, Rio de Janeiro, 22221140, Brazil,* Antonio E. Nardi

Educational Objectives:

At the conclusion of this presentation, the participants should be able to recognize the importance of the recognition and early treatment of mood and anxiery disorders among women attending in perimenopause outpatient clinics. Women in Brazil between 45 and 55 years old with mild mental disorders usualy look for gynecologic clinics. Our results reflect this data and there is a need of a crescent interaction between this public, gynecologists and psychiatrists to increase mental disorders detection and psychiatric treatment offer for conditions that are highly disruptive of women's life quality.

Summary:

Objective: To determinate the prevalence of depressive-anxiety disorders among women in a perimenopause outpatient clinic since Brazilian data are little and contradictory. **Methods:** Eighty six women attending in the perimenopause clinic of the Gynecology Institute of Federal University of Rio de Janeiro were assessed trough the MINI interview. **Results:** The majority of women had a psychiatric disorder (57%) with highest prevalence for GAD (34,9%) and Major Depression (31,4%). The group with any disorder was represented for younger, married, lower school education and positive family history for psychiatric disorder in women. There is a higher prevalence of psychiatric disorder among outpatient woman attending in menopause clinics as observed in out trial than among outpatient women attending in general clinics as described in the literature. The high co-morbidity prevalence (55,5% of patients with any disorder) complicating the primary disorder may compromise the prognosis of most patients and reflect the lack of early specific treatment for mental disorders among assessed women. **Conclusion:** We observed the need of a crescent interaction between this public, gynecologists and psychiatrists to increase mental disorders detection and psychiatric treatment offer for conditions that are highly disruptive of women's life quality.

References:

1. Ballinger CB. Psychiatric morbidity and the menopause: survey of a gynaecological out-patient clinic. Br J Psychiatry. 1977;131:83-9.
2. Gater R, Tansella M, Korten A, Tiemens BG, Mavreas VG, Olatawura MO. Sex differences in the prevalence and detection of depressive and anxiety disorders in general health care settings: report from the World Health Organization Collaborative Study on.

NR869 Wednesday, May 24, 3:00 PM - 5:00 PM

Gaboxadol Improves Sleep Onset and Maintenance and Enhances Low Frequency Components of NREM Sleep EEG in a Model of Transient Insomnia

James K. Walsh *St. Luke's Hospital, 232 S. Woods Mill Road, Chesterfield, MO, 63017*, Steve Deacon, Ph.D., Derk Dijk, Ph.D., Jonas Lundahl, Ph.D.

Educational Objectives:

The participants will gain knowledge on the effect of Gaboxadol on the sleep onset and maintenance in patients with transient insomnia.

Summary:

Objective: Gaboxadol is a selective extrasynaptic Gamma-aminobutyric acid $_A$ agonist (SEGA) that has demonstrated improvements in both sleep onset and maintenance measures in patients with insomnia. The present study was designed to evaluate the efficacy of gaboxadol in a model of transient insomnia.

Methods: 109 healthy subjects (18-58 y) completed a randomized, double-blind, crossover study in a 4h phase advance model of transient insomnia. Sleep was assessed using polysomnographic (PSG) and self-reported measures following gaboxadol 5, 10 and 15mg (GBX5, GBX10, GBX15) versus placebo (PBO). Zolpidem 10 mg (ZOL10) was used as an active reference.

Results: Efficacy analysis was based on 82 per protocol subjects. Wakefulness after sleep onset (WASO) and total sleep time (TST) were significantly improved in all active treatments compared with PBO (WASO-all $p<0.05$; TST-all $p<0.001$), with no apparent dose response for gaboxadol. Latency to persistent sleep was significantly shorter than PBO for GBX10 and GBX15 (both $p<0.05$) and ZOL10 ($p<0.001$), but not with GBX5. GBX10 and GBX15 increased ($p<0.05$) slow-wave (SWA; 0.75-4.5 Hz) and theta (4.75-7.75 Hz) activity in NREM sleep EEG in a dose dependent manner. In contrast, zolpidem did not enhance SWA ($p=0.8$) and reduced theta activity ($p<0.0004$). Self-reported (s) measures of sleep maintenance showed improvements in both sWASO ($p<0.05$) and sTST ($p<0.05$) for all active treatments compared with PBO. Self-reported sleep onset was significantly reduced following all active treatments except GBX5. Neither drug treatment was associated with residual effects at 30 minutes or 3 hours after lights-on. The majority of adverse events were mild or moderate with no SAEs. **Conclusion:** Gaboxadol 10mg and 15mg improved sleep on PSG and self-reported efficacy measures in this model of transient insomnia. In contrast to zolpidem, gaboxadol enhances low frequency components of sleep EEG. There were no next day residual effects and the treatments were well tolerated.

References:

1. Storustovu S, Ebert B. Gaboxadol: in vitro interaction studies with benzodiazepines and ethanol suggest functional selectivity. Eur J Pharmacol. 2003 Apr 25;467(1-3):49-56.
2. Deacon, S., Staner, L., Staner C., Vorstrup, S. and Lundahl J. Acute administration of gaboxadol improves sleep initiation and maintenance in patients with primary insomnia [abstract]. Sleep, Vol 28, 2005.

NR870 Wednesday, May 24, 3:00 PM - 5:00 PM

A National Survey of Psychotherapy Training in Psychiatry, Psychology,and Social Work

Myrna M. Weissman, Ph.D. *Columbia University, Psychiatry, 1051 Riverside Drive, Unit 24, New York, NY, 10032-2603*, Helen Verdeli, Ph.D., Marc J. Gameroff, Ph.D., Sarah E. Bledsoe, M.S.W., Kathryn Betts, Ph.D., Laura Mufson, Ph.D., Priya Wickramaratne, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand the most frequent evidence based and non-evidence based psychotherapies taught in psychiatric residencies and graduate programs in psychology and social work. They will know whether these psychotherapies are optional or are required.

Summary:

Approximately 3% of the US population receives psychotherapy each year from psychiatrists, psychologists or social workers. A modest number of psychotherapies are evidence based (EBT) in that they have been defined in manuals and found efficacious in at least 2 controlled clinical trials with random assignment. Few practioners use EBT.

A survey of a probability sample of all U.S. accredidated training programs in psychiatry, psychology and social work was completed to determine the amount of EBT taught in; whether the training was elective or required, presented as a didactic (coursework) or clinical supervision. The findings show that programs offer electives in a range of EBT and non-EBT, few require both a didactic and clinical supervision in EBT, and most of required training is non-EBT. Psychiatry required coursework and clinical supervision in the largest percent of EBT (28%). Cognitive behavioral therapy was the EBT most frequently offered and required as a didactic in all three disciplines. Over 90% of the psychiatry training programs are complying with the new Cognitive-Behavior Therapy requirement. The two disciplines with the largest number of students and emphasis on clinical training_professional clinical psychology (Psy.D.) and social work_had the largest percentage of programs (67% and 62%, respectively) not requiring a didactic and clinical supervision in any EBT. Until the training programs in the major disciplines providing psychotherapy increase training in EBT, the gap between research evidence and clinical practice will remain.

References:

1. Roth A, Fonagy P: What Works For Whom? A Critical Review of Psychotherapy Research. London, Guilford, ed. 2, 2004.
2. Gabbard GO: Evaluating Core Competencies in Long Term Psychodynamic Psychotherapy. In Long Term Psychotherapy: A Basic Text. Washington, DC, American Psychiatric Publishing, 2004, chap. 11.

NR871 Wednesday, May 24, 3:00 PM - 5:00 PM

Plasma Prolactin Levels During Cocaine Withdrawal

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Educational Objectives:

At the conclusion of this presentation, the participants should be able to:

1. Understand the use of plasma prolactin levels as a peripheral marker of dopamine function.

2. Be familiar with the effect of cocaine use on hormone function.

Summary:

Plasma prolactin levels have been used as a peripheral marker of dopamine function in the study of cocaine addiction because dopamine receptor activation inhibits prolactin release. Published studies are inconsistent regarding initial and subsequent prolactin levels during cocaine withdrawal. We addressed this issue by measuring plasma prolactin levels by radioimmunoassay in 84 physically healthy male cocaine addicts (mean [SD] age 34.8 [7.4] years, 7.3 [5.2] years of cocaine use, no other current psychiatric or substance use disorder except tobacco dependence) at the start of 4 weeks of inpatient treatment (last cocaine use 7.8 [10.2] days before), 42 of whom also provided samples after 8, 14, and 27 days of monitored abstinence. Subjects were randomly assigned to receive the dopamine receptor agonist bromocriptine (1.25-7.5 mg/day) or placebo double-blind starting after blood sampling on day 14. The initial (day 1 or 2) prolactin level was 8.5 [4.8] ng/ml. There were no significant correlations between initial prolactin level and subjects' age, years of cocaine use, or measures of recent cocaine use. Subjects receiving placebo (n = 21) showed no significant change in subsequent prolactin levels. Subjects receiving bromocriptine (n = 21) showed no significant change until day 27 (2 weeks on medication), when there was significant suppression of prolactin level (1.7 [3.2] ng/ml, $p < 0.001$). These findings suggest there are no significant effects of chronic cocaine use or cocaine withdrawal on basal plasma prolactin levels or response to bromocriptine. Reasons for the difference from some (but not all) previously published studies are unclear, but may include this study's larger sample size and inclusion of subjects without any comorbidities except tobacco dependence.

Supported by Novartis Pharmaceuticals Co. and the Intramural Research Program of the National Institutes of Health, National Institute on Drug Abuse.

References:

1. 1. Elkashef A & Vocci F: Biological markers of cocaine addiction: implications for medications development. Addict.Biol 2003; 8:123-139.

2. 2. Contoreggi C, Herning RI, Koeppl B, Simpson PM, Negro PJ Jr., Fortner-Burton C, Hess J: Treatment-seeking inpatient cocaine abusers show hypothalamic dysregulation of both basal prolactin and cortisol secretion. Neuroendocrinol 2003; 78:154-162.

NR872 Wednesday, May 24, 3:00 PM - 5:00 PM

Involving Residents in Person-Centered Culture Change

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to 1) discuss "person-centered care" as an over-riding value for patient care, particularly as it applies to inpatient psychiatric care, 2) describe the involvement of psychiatric residents in person-centered culture change on a psychiatric inpatient unit, 3) discuss the integration of person-centered values in psychiatric residency training.

Summary:

The acute inpatient psychiatric service ("One Northwest") at Oregon Health & Science University adopted the value of "Person Centered Care" several years ago. Participation in the "Creating Violence Free and Coercion Free Mental Health Treatment Environments Project" sponsored by the National Association of State Mental Health Program Directors gave additional impetus to change the unit culture and practice, resulting in further reductions, and near elimination, of seclusion and restraint. Psychiatric Residents at various levels of training have been integral members of the interdisciplinary process that has been bringing about these changes. This poster outlines the ways that junior and senior level residents have been involved in the process both as learners and as active participates in culture change, and how "person-centered" values are now integrated into the residency training on the unit. Data are presented regarding changes in objective measures of change as rates of seclusion. Educational objectives and methods are presented from the perspective of the unit's Medical Director and Program Director. A psychiatric resident presents a case vignette that demonstrates her experience with "patient centered culture change." Involving residents in the process of culture change has educational benefits as well as contributing to advances in clinical care.

References:

1. Hagenow NR: Why not person-centered care? Nursing Admin Quart. 2004; 27(3):203-207.

2. NASMHPD Medical Directors Council. Reducing the use of seclusion and restraint, Alexandria VA: National Association of State Mental Health Program Directors, July, 1999.

NR873 Wednesday, May 24, 3:00 PM - 5:00 PM

Dysthymic Disorder, Response to Venlafaxine, and Monoamines in Lymphocytes

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Educational Objectives:

The objectives of the present research were:

1. To explore the nervous-immune interaction in major depression patients
2. To determine basal proliferation of lymphocytes in major depression
3. To understand the role of serotonin in the process of lymphocyte proliferation thinking in autoimmunity and depression
4. To evaluate populations of lymphocytes with differential function and the serotonergic system
5. To highligth the relevance of possible immune modifications an the treatment of depression
6. To study the response to treatment with venlafaxine
7. To test the sensibility of the Computerised Diagnosis Interview for Psychiatry
8. To train Residents in New Research

Summary:

Dysthymic patients present several immune alterations, related to chronic evolution. This study includes 27 patients, 18-60 years, diagnosis with the Computerised Diagnosis Interview for Psychiatry, and 19 controls. They received venlafaxine 75-150 mg/day for 6 weeks. Lymphocytes from peripheral blood were isolated by density gradients with Ficoll/Hypaque. Monoamines and their metabolites were determined by HPLC with electrochemical detector in platelet poor plasma and in lymphocytes. 5HT transporter in lymphocyte membranes was labeled with [^{3}H]paroxetine. There was a good clinical response to venlafaxine with reduction of Hamilton Scale for Depression greater than 50%. 3,4-Dihidroxifenilacetic acid was increased in the plasma. 5HT and noradrenaline

turnover rates, expressed as the ratio monoamine/metabolite, were unmodified, but that of dopamine was diminished in lymphocytes of patients. There was a reduction of about 80% in the number of 5HT transporters, greater than that reported for major depression episodes. The CIDI resulted efficient instrument for detection of dysthymia, venlafaxine was effective, and, in this group of patients, there was an alteration of dopamine system in lymphocytes, cells that possesses dopaminergic receptors which could influence immune functionality.

References:

1. Urbina M, Pineda S, Piñango L, Carreira I, Lima L. [3H]Paroxetine binding to human peripheral lymphocyte membranes of patients with major depression before and after treatment with fluoxetine. Int J Immunopharmacol 1999 21:631-646.
2. Effect of mirtazapine treatment on serotonin transporter in blood peripheral lymphocytes of major depression patients. Int Immunopharmacol 2005, 5:1069-1079.

NR874 Wednesday, May 24, 3:00 PM - 5:00 PM

Nocturnal Eating Behavior Related to Zoplidem

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Educational Objectives:

Hoping clinically, we report 4 cases of nocturnal eating behavior related to zolpidem therapy. The patients started suddenly nocturnal eating behavior with partial or no recall after zolpidem medication over 10 months. In addition, with discontinuation or reducing the dosages of zolpidem, the subsequent resolution of eating behavior was observed. This finding strongly suggests the relationship between zolpidem and the nocturnal eating episode.

Summary:

Objective: We have experienced 4 cases of nocturnal eating behavior when zolpidem therapy was begun for insomnia and the subsequent resolution of eating behavior with discontinuation of zolpidem.

Case1: A 57-year-old woman with DSM-IV depressive episode had taken zolpidem 10mg and fluoxetine 20mg for 21 months. Suddenly she complained an uncontrollable desire to eat began after 2 hours of sleep onset. She could remember most of the eating episodes. After reducing the dosage of zolpidem to 5mg, eating episodes were disappeared. Case 2: A 28-year-old woman with the diagnosis of DSM-IV schizophrenia, had taken zolpidem 10mg and risperidone 6mg for 10 months. She awoke 1 hour after sleep onset and wandered around with partial recall. As soon as the discontinuation of zolpidem, she no longer had eating episodes or partial amnesia. Case 3: A 43-year-old woman with DSM-IV schizophrenia had taken risperidone 6mg and zolpidem 10mg. After 38 months of zolpidem medication, she suddenly started to awake 2 hours after sleep onset and ate something or went outside with partial recall. Stopping zolpidem had made her free of eating and sleepwalking episode in a day. Case 4: A 34-year-old man with DSM-IV schizophrenia had taken risperidone 4-8mg and zolpidem 10mg. In 55 months of zolpidem medication, he awoke 2 hours after sleep onset and ate snack with no recall. After one week, zolpidem was discontinued and the nocturnal eating episodes stopped.

Conclusions: The patients with zolpidem medication over 10 months, suddenly started nocturnal eating episodes 1-2 hours after sleep onset with partial or no recall. They reported the stopping of the eating episode within 1-2 days after discontinuation or reducing of zolpidem. This finding strongly suggests the relationship between zolpidem and the nocturnal eating episode. The sleep specialist should be aware that zolpidem may contribute to nocturnal eating behavior.

References:

1. Timothy I. Morgenthaler, Michael H. Silber: Amnestic sleep-related eating disorder associated with zolpidem. Sleep Med 2002; 3:323-327.
2. Mendelson WB: Sleepwalkng associated with zolpidem (see comments). J Clin Psychopharmacol 1994; 14(2):150.

NR875 Wednesday, May 24, 3:00 PM - 5:00 PM

Involuntary Commitment Influences Perceptions of Coercion in Psychiatrically Hospitalized Veterans

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Educational Objectives:

At the conclusion of this presentation, the participant should learn about factors associated with perceptions of coercion in hospitalized psychiatric patients, and the importance of policies that aim to reduce coercive treatment experiences among hospitalized psychiatric patients.

Summary:

Objective: Increased perceptions of coercion in psychiatric patients may be associated with poorer outcomes by impairing appropriate and timely service-seeking due to fear of involuntary commitment. However, there is little research on factors related to perceived coercion in veterans. The present analysis examines whether current involuntary commitment and lifetime history of coercive experiences during hospitalization are associated with higher levels of perceived coercion in psychiatrically hospitalized veterans.

Method: Participants were consecutively consented psychiatric inpatients diagnosed with a severe mental illness (SMI), recruited from March 2004-August 2005 at the Durham VAMC (N-211). Perceived coercion was measured with the 15-item Admission Experience Survey. Treatment history, clinical, and socio-demographic variables were assessed via record review and self-report. Negative binomial regression was used to examine the relationship between perceived coercion and involuntary commitment, adjusting for other variables.

Results: The average age of the sample was 50 years (SD= 9), 34% white, 88% male, and 31% married or in a committed relationship. The median number of coercive statements reported in the sample for the current admission was 1 (first quartile = 0, third quartile = 4), with a range of 0 to 14. Seventeen percent were currently involuntarily committed. By self-report, lifetime history of coercive treatments were as follows: 40% prior involuntary commitment, 33% placed in seclusion, 30% placed in physical restraints, 24% forced to take medication against their will, and 30% denied medication asked for and felt they needed. Factors related to perceived coercion in unadjusted analyses ($p<0.10$) include current involuntary commitment, ever forced medications, ever denied medications, psychiatric diagnosis, male gender, and subjective social support. In adjusted analyses, patients whose current admission was involuntary reported significantly higher levels of coercion (Incidence rate ratio= 2.55; 95% CI = 1.57-4.12; $p = 0.0001$).

Conclusion: Current involuntary commitment was significantly related to perceptions of coercion.

References:

1. Swartz MS, Wagner HR, Swanson JW, Hiday VA, Burns BJ: The Perceived Coerciveness of Involuntary Outpatient Commitment: Findings from an Experimental Study. J Am Acad Psychiatry Law 2002;30:207-217.
2. Swanson JW, Swartz MS, Hannon MJ, Elbogen EB, Wagner HR, McCauley BJ, Butterfield MI: Psychiatric Advance Directives: A Survey of Persons With Schizophrenia, Family Members, and Treatment Providers. Int J Forensic Ment Health 2003; 2:73-78.

NR876 Wednesday, May 24, 3:00 PM - 5:00 PM

A Review of Health-Related Quality of Life Instruments in Alcohol Dependent

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to summarize the quality of life instruments used in alcohol dependence.

Summary:

Introduction: Alcohol dependence (AD) has broad impact on many areas of patient quality of life (QOL) including emotional functioning, social functioning, and activities of daily living. Using a valid and reliable instrument to measure the impact on QOL is critical for any clinical trial evaluating a treatment for AD. A literature review was conducted to identify QOL instruments that have been used in alcohol dependent patients.

Methods: We conducted a literature search in Medline and Embase databases to identify QOL publications in alcohol dependence since 1990.

Results: Out of 596 abstracts reviewed, only 23 articles examined QOL instruments in alcohol dependence. Nine generic QOL instruments had been used in AD studies since 1990, while no disease-specific QOL instrument was found. The Short-Form 36 (SF-36) was the most frequently used instrument (6 studies). Most of the instruments were responsive to changes in AD with treatment, and demonstrated improvement in QOL, particularly in social life, relationships, emotional well-being, and work functioning. Two problems were noted in the review of the generic instruments in AD: (1) the generic measures may not adequately capture specific information relevant to this population (e.g., domains covering social isolation and craving), and (2) the questionnaires have never been psychometrically tested in an AD patient population.**Conclusions:** Generic QOL instruments are responsive and may be appropriate for use in AD patients after further evaluation and testing. There is a need for a disease-specific QOL instrument that includes domains specific to AD and is likely to be more sensitive than generic measures.

References:

1. Ware J Jr, Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. Medical Care 1996; 34(3):220-33.
2. Coons SJ, Rao S, Keininger DL, Hays RD, A comparative review of generic quality-of-life instruments. Pharmacoeconomics 2000; 17(1):13-35.

NR877 Wednesday, May 24, 3:00 PM - 5:00 PM

Prevalence and Diagnostic Correlates of *DSM-IV* Pathological Gambling in Psychiatric Outpatients

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Educational Objectives:

At the conclusion of this presentation the participant should be able to describe the prevalence of DSM-IV pathological gambling in psychiatric outpatients, and the diagnostic correlates of gambling.

Summary:

Background: Studies of the prevalence of pathological gambling (PG) in psychiatric and substance abusing patients suggest that the disorder is not rare. Most studies have been of substance abusers in treatment, and the rate of PG has been found to be several times higher than the rate found in community based epidemiological surveys. However, only one study has examined the prevalence of PG in a heterogeneous sample of patients, and this was a study of psychiatric inpatients. We are not aware of any prior study of the prevalence of PG in a psychiatric outpatient sample. In the present report from the Rhode Island Methods to Improve Diagnosis and Services (MIDAS) project we examined the current and lifetime prevalence of PG in psychiatric outpatients. **Methods:** 1,709 psychiatric outpatients were interviewed with a semi-structured diagnostic interview that included a module to diagnose DSM-IV PG. **Results:** Forty (2.3%) patients had a lifetime history of DSM-IV PG, all of whom had at least one other DSM-IV axis I disorder. Patients with PG had significantly more Axis I disorders than patients without PG, and had significantly higher rates of bipolar disorder, social phobia, panic disorder with agoraphobia, alcohol use disorder, and other impulse control disorders. **Conclusions:** PG was rarely diagnosed in a psychiatric outpatients. Possible reasons for the low prevalence of PG in our sample are discussed.

References:

1. Lesieur, H., Blume, S. (1990). Characteristics of pathological gamblers identified among patients on a psychiatric admissions service. Hospital and Community Psychiatry, 41, 1009-1012.
2. Ibanez, A., Blanco, C., Donahue, E., Lesieur, H., de Castro, I., Fernandez-Piqueras, J., Saiz-Ruiz, J. (2001). Psychiatric comorbidity in pathological gamblers seeking treatment. American Journal of Psychiatry, 158, 1733-1735.

NR878 Thursday, May 25, 12:00 PM - 2:00 PM

Facial Affect Recognition: A Mediator Between Cognitive and Social Functioning in Psychosis?

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Educational Objectives:

The participant will understand the role of facial affect recognition in the relationship between cognition and social functioning in schizophrenia.

Summary:

Objective: Facial affect recognition has been implicated in the relationship between cognition and social functioning. Individuals with schizophrenia have demonstrated impairments in all three domains (Addington & Addington, 1998; 2000). This one-year longitudinal study tested the hypothesis that facial affect recognition mediates the relationship between cognitive and social functioning. *Method:* Three groups were included: 50 first-episode of psychosis (FE) subjects, 53 multi-episode schizophrenia subjects (ME) and a non-psychiatric comparison group (NPC) (n=55). Subjects were assessed on two facial affect recognition tasks, a comprehensive cognitive battery and a measure of social functioning. First episode subjects were assessed on admission to a comprehensive FE program and one year later. The ME and NPC group also had 2 assessments one year apart. *Results*: There were

minimal if any changes over time for all groups on the measures. The exception was that FE subjects improved in symptoms and social functioning over the first year. Results of ANOVAs demonstrated that both the FE and ME subjects were clearly impaired relative to NPCs in cognition, social functioning and facial affect recognition. There were significant associations among facial affect recognition, cognition and social functioning in all three groups. A series of regression analyses were performed according to the method outlined by Baron and Kenny (1984) to determine if facial affect did indeed mediate the relationship between cognitive and social functioning. Results were that for the NPC group facial affect did not mediate the relationship. However in the patient group there was evidence that facial affect recognition did partially mediate the relationship between cognitive and social functioning. *Conclusion:* This is a first step in understanding the complex relationship between cognition and outcome and could potentially have implications for the design of remediation strategies.

References:

1. Addington J. & Addington D: Facial affect recognition and information processing in schizophrenia and bipolar disorder. Schiz Res 1988: 32:171-181.
2. Addington J, Saeedi H, & Addington D. The course of cognitive functioning in first episode psychosis: Changes over time and impact on outcome. Schiz Res 2005: 78: 35-43.

NR879 Thursday, May 25, 12:00 PM - 2:00 PM

Substance Use in Early Psychosis: A Three-Year Follow-Up

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Educational Objectives:

At the conclusion of the presentation the participant will have knowledge about the prevalence of substance misuse in early psychosis.

Summary:

Background: Substance misuse is a significant problem in schizophrenia. The purpose of this study was to examine the prevalence and correlates of substance misuse in individuals with a first episode of psychosis for three years following their admission to a specialized early psychosis program. *Method:* 203 subjects (142 men, 61 women) were included in the study. Assessment measures were the Positive and Negative Syndrome Scale, the Calgary Depression Scale for Schizophrenia, the Quality of Life Scale, and the Case Manager Rating Scale. Assessments were conducted at baseline and at 1, 2 and 3 years. *Results:* At baseline 47% of the sample, the majority of whom used alcohol or cannabis met diagnostic criteria for substance abuse/dependence. This number was reduced to 32% by one year. This prevalence is significantly higher than in the general population. There was a significant reduction in use of alcohol over the three years with most change occurring in the first year (35% to19% abusing). For cannabis use there was continual reduction over the first 2 years (35% to 7% abusing). At all times high levels of cannabis and alcohol use were significantly associated with male gender, young age and age of onset. There was no association between alcohol abuse and symptoms or functioning. However, cannabis abuse was significantly associated with depression and positive symptoms across time. *Conclusions:* This study confirms the high rates of substance misuse, in particular cannabis, in first-episode psychosis. However this decreases significantly overtime within this specialized program. Regardless of decline in numbers using, cannabis misuse is consistently associated with severity of symptoms.

References:

1. van Mastrigt S. Addington J. & Addington, D. Substance misuse at presentation to an early psychosis program. Soc Psych Psychiatric Epidem 2004: 39: 69-72.
2. Verdoux H, Tournier M & Cougnard A. Impact of substance use on the onset and course of early psychosis. Schiz Res: 79:69-75.

NR880 Thursday, May 25, 12:00 PM - 2:00 PM

Neuropsychological Tests That Accurately Discriminate the Preclinical Alzheimer's Disease

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that the individuals who complain subjective memory impairment have an increased risk of future dementia. Thus it is important to evaluate periodically cognitive function and related symptoms using the reliable and objective instrument.

Summary:

Objectives: It is well known that AD pathology in the brain has appeared before the clinical onset of dementia. The purpose of this study is to explore the cognitive impairment, functional decline, and behavioral problems among the preclinical AD.

Methods: 34 non-demented subjects who visited at Geropsychiatry Clinic, Department of Psychiatry were included in the study. They completed baseline clinical evaluation and neuropsychological test battery assessing various cognitive functions, activities of daily living, and behavioral problems. 11 subjects were ultimately diagnosed with AD according to DSM-IV after 0.5 to 2 years (mean 1.1 years) baseline and 23 subjects remained non-demented throughout the 3 years of follow-up.

Results: The subjects who subsequently developed AD performed more poorly than non-demented at baseline on the Korean-Rey Auditory Verbal Learning Test (K-AVLT) Word List Immediate Recall, Delayed Recall, Delayed Recognition, Korean-Rey Complex Figure Test (K-CFT) Immediate Recall, Delayed Recall, and Korean-Boston Naming Test (K-BNT). Among the 17 neuropsychological tests, the K-AVLT Word List Total Learning Trial (AUC= .864) discriminated best between subjects diagnosed with AD and non-demented, followed by the K-BNT (AUC=.792), Animal Fluency (AUC=.762), K-CFT Delayed Recall (AUC=.745) and Immediate Recall (AUC=.740), K-AVLT Word List Delayed Recognition (AUC=.729) and Delayed Recall (AUC=.716).

Conclusions: Our results confirm that cognitive impairment can be detected well before clinical onset of AD. Memory, naming ability, and word fluency measures discriminated the most accurately between preclinical AD and subjects who remained non-demented. On the other hand, cognitive functions that decline later in the disease process, such as visuospatial or frontal/executive function, would be less useful predictors of early AD. These findings are consistent with the commonly accepted view that some of the earliest brain changes in AD occur in the medial temporal lobe structures. Our findings have implications for the early detection of AD, and prevention and early intervention.

References:

1. Saxton J, Lopez OL, Ratcliff G, Dulberg C, Fried LP, Carlson MC, Newman AB, Kuller L. Preclinical Alzheimer disease Neu-

ropsychological test performance 1.5 to 8 years prior to onset. Neurology 2004; 63:2341-2347.

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NR881 Thursday, May 25, 12:00 PM - 2:00 PM

Route Learning Impairment Associated With Encephalomalasia Secondary to Head Trauma

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Educational Objectives:

This report demonstrated that primary disability after a head trauma could be a neuropsychological disorder and a complete neuropsychological is needed for determining the cognitional sequels of trauma. Main disabilities of our patient such as inability to visit hospital alone, requirement of an escort to the out of his town by others or getting lost frequently in newly learned environments were resolved within six month after an individualized neuropsychological management strategy. Therefore, constitution of an individualized handling strategy for increasing quality of life of patients with topographical disorientation is the most critical part of the management.

Summary:

Topographical disorientation is difficulty to find one's way in familiar or new environments. We report on a 30-year-old male developed difficulty in learning of new routes following a head trauma, but the navigation in familiar surroundings was intact. Magnetic resonance images revealed bilateral parahippocampal and occipital encephalomalasia. Neuropsychological evaluation showed impairment in acquisition of new topographical spatial knowledge and representation of spatial value of landmarks with preserved ability to learn visual and verbal information of them. This is the first report in the literature that describes route learning impairment associated with encephalomalasia of parahippocampal region secondary to head trauma. In this case, the increased anxiety and the inappropriate visual inputs resulted from right homonymous hemianopsia, decreased visuospatial ability due to cervical dystonia, and an attention deficit caused by involvement of temporo-occipital junctions also appears to role in this impairment also. The importance of management strategies including educational procedures depended upon left temporal lobe functions were also underlined.

References:

1. Epstein R, Harris A, Stanley D, Kanwisher N. The parahippocampal place area: recognition, navigation, or encoding? Neuron. 1999 May;23(1):115-25.

2. Maguire EA. The retrosplenial contribution to human navigation: a review of lesion and neuroimaging findings. Scandinavian Journal of Psychology. 2001; 42: 225-238.

NR882 Thursday, May 25, 12:00 PM - 2:00 PM

Influence of Low Dose Risperidone in Elderly Patients With Dementia on Serum Lipids and Mortality

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the usefulness of risperidone in the treatment of impulsive disorders associated to dementia, especially low dose in elderly patients, and the lack of association to increased levels of serum lipids during the treatment nor cardiovascular motality.

Summary:

Aim: Impulsive disorders affect commonly elderly patients with dementia. Risperidone has been involved in developing acute stroke and lipid disorders. We study the effect of low dose risperidone on serum lipids and its relationship with mortality, especially cardiovascular mortality.

Methods: 31 patients were investigated. Total cholesterol, LDL, HDL and triglycerides were measured at baseline and after 3 months of starting risperidone (1mg/day) for controlling impulsiveness. Mortality was assesed after 6 months of follow-up.

Results: 18 patients were women and 13 men. Middle age 80.65 +/- 8.66 years-old. At baseline, total cholesterol was 188.90 +/- 48.33; LDL 129.25 +/- 39.54; HDL 41.93 +/- 13.90 and triglycerides 111.51 +/- 50.35. After 3 months total cholesterol was 190.35 +/- 56.01 (p=0.822); LDL 130.61 +/- 49.52 (p=0.808); HDL 45.74 +/- 13.42 (p=0.180) and triglycerides 108.16 +/- 45.22 (p=0.685). Al results are shown in mg/dl. After 6 months, 7 (22.58%) patients died. One patient died after suffering stroke and the other 6 from malignancy (2) and infectious diseases (4). No patient died during the first 3 months of the study.

Conclusions:

1.- Low dose risperidone is useful in elderly patients with impulsive disorders and dementia.

2.- Risperidone did not change significantly serum lipids after 3 months in these patients.

2.- After 6 months of follow-up, only one patient died from cardiovascular disease. The other 6 died from infectious diseases and malignancy.

References:

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2. Sink KM, Holden KF, Yaffe K. Pharmacological treatment of neuropsychiatric symptoms of dementia: a review of the evidence. JAMA. 2005 Feb 2;293(5):596-608.

NR883 Thursday, May 25, 12:00 PM - 2:00 PM

The Physician Patient Relationship in Cosmetic Surgery: A Patient Perspective

Antonia L. Baum, M.D. *George Washington University, 5522 Warwick Place, Chevy Chase, MD, 20815*, Bruce M. Freedman, M.D., Elizabeth L. O'Hara, R.N.

Educational Objectives:

At the conclusion of this presentation the attendee should be able to better understand the nature of the physician patient relationship in cosmetic surgery.

Summary:

Objective: The purpose of this study was to examine whether the traditional boundaries between physicians and patients as perceived by the patients are being changed in the field of cosmetic surgery.

Methods: 100 consecutive patients (82 women; 18 men) who presented for consultation in a cosmetic surgery office were surveyed about the physician patient relationship. The questionnaire focused on the appropriateness of a cosmetic surgeon to perform procedures on people with whom there was a personal relationship (i.e. spouse, parent, significant other).

Results: Of the patients surveyed, 80% indicated that it was inappropriate for a cosmetic surgeon to perform a surgical procedure (i.e. facelift, liposuction) on someone with whom they were personally involved. 20% of patients surveyed believed that it was inappropriate for a cosmetic surgeon to perform a non-surgical procedure (i.e. BOTOX, Restylane) on someone with whom they were personally involved. The difference was statistically significant ($P < 0.01$). There was a gender difference in that the majority of male subjects (3:1) did not see surgical intervention as inappropriate.

Conclusion: In evaluating the appropriateness of cosmetic surgeons performing procedures on people with whom they were personally involved, patients surveyed in this study noted a distinction between surgical and non-surgical procedures. The majority believed that non-surgical procedures were acceptable while surgical procedures were not acceptable. In psychiatry, the physician patient relationship is unambiguous. However, this appears to be changing in the field of cosmetic surgery, where commercialization may be affecting patients' attitudes about what constitutes medical treatment. This may have important forensic and patient care implications.

References:

1. Hasan JS: Psychological issues in cosmetic surgery: a functional overview. Ann Plast Surg 2000:44;89-96.
2. Borah G, Rankin M, Wey P. Psychological complications in 281 plastic sugery practices. Plast Reconstr Surg 1999:104;1241-6.

NR884 Thursday, May 25, 12:00 PM - 2:00 PM

Cosmetic Surgery and the Use of Antidepressant Medication

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Educational Objectives:

At the conclusion of this presentaion the atendee should be able to understand the association of cosmetic surgery and the use of antidepresant medication.

Summary:

Objective: The purpose of this study was to determine whether antidepressant use was affected by the performance of cosmetic surgery.

Methods: Over a twelve month period, 362 consecutive patients undergoing elective cosmetic surgery were questioned regarding their use of antidepressant medications. Six months following surgery, patients were surveyed on their use of antidepressant medications, and whether the surgery had changed "the way they felt about themselves."

Results: Of the 362 patients, 83% (Group A, n=301) were not taking antidepressants preoperatively, and 17% (Group B, n=61) were taking antidepressants preoperatively. The two groups were similar regarding age, gender, and types of surgery performed. Post-operatively, 5% (N=15) of the 301 patients in Group A began taking antidepressants after surgery, a 4% change in antidepressant use. In group B, 42 of the 61 patients on antidepressants before surgery were still taking them post-operatively; this represented a 31% decrease in antidepressant use. The differences in antidepressant use were statistically significant (P<.05). 99% of patients in group A and 98% of patients in group B claimed that the cosmetic surgery had "improved" their self esteem.

Conclusion: In this study, there was a 31% decrease in the use of antidepressant medication taken after a cosmetic procedure. While the etiology of anxiety and depression is multifactorial, this study suggests the possibility that cosmetic surgery may influence the use of antidepressant medication.

References:

1. Sarwer DB, Zanville HA, LaRossa D, Bartlett SP, Chang B, Low DW, Whitaker LA: Mental Health Histories and psychiatric medication usage among persons who sought cosmetic surgery. Plast Reconstr Surg 2004;114:1927-33.
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NR885 Thursday, May 25, 12:00 PM - 2:00 PM

The Prevalence of Thyroid Dysfunction in Schizophrenia

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Educational Objectives:

At the conclusion of this presentation the particpant should be able to: 1) recognize the importance of access to care for comorbid physical illness, 2) realize the importance of including patients with schizophrenia in health care initiatives for the general population.

Summary:

Objective: Thyroid dysfunction has been linked to mood disorders. Schizophrenia has been associated with greater rates of metabolic disorders. The study goal was to evaluate the prevalence of thyroid dysfunction in schizophrenia and the relationship to antipsychotics.

Method: Included a chart review of all inpatients of two state psychiatric hospitals (N=448). All subjects had a medical history, physical exam and screening blood tests. Lithium treatment was excluded. Subjects were compared to general population (GP).

Results: Subject Characteristics: 39 + 5 years (18-87); 284 males, 405 Patients with Schizophrenia. Prevalence: Hypothyroidism was 15.7% (4.6% GP); 9.1% treated, 6.6% subclinical. Hyperthyroidism was 2% (1.3% GP);1.5% treated, 0.5% subclinical. Comorbid physical illness in treated hypothyroidism; 21.6% diabetes, 35.1% hypercholesterolemia, 10.8% cardiovascular disease, 16.2% hypertension and subclinical hypothyroidism; 33.3% hypercholesterolemia, 22.2% hypertension. Data did not suggest a link between specific antipsychotic treatment and thyroid dysfunction.

Conclusion: Thyroid dysfunction in schizophrenia was significantly greater (chi square= 27.2,df=1, P<.0001) than the general population. The sample size limits our ability to make population inferences yet there appears to be an association between schizophrenia and thyroid dysfunction. Findings suggest that improvements in comprehensive psychiatric care should include routine screening for thyroid function, diabetes, hypertension, and hypercholesterolemia.

References:

1. Hollowell JG, et al: Serum TSH, T4 and Thyroid Antibodies in the United States Population (1988 to 1994): National Health and Nutrition Examination Survey (NHANES III). J Clin Endocrinol Metab, February 2002, 87(2):489-499.
2. Kelly DL, Conley RR: Thyroid function in treatment-resistant schizophrenia patients treated with quetiapine, risperidone, or fluphenazine. J Clin Psychiatry 2005 Jan;66(1):80-84.

NR886 Thursday, May 25, 12:00 PM - 2:00 PM

Donepezil Treatment of Severe Alzheimer's Disease: Results From a 24-Week, Multinational, Placebo-Controlled Trial

Sandra Black, M.D. *Sunnybrook and Women's College, Neurology, Cognitive Neurology A421, 2075 Bayview Avenue, Toronto, ON, M4N 3M5, Canada*, Honglan Li, Ph.D., Tom McRae, M.D., Sharon Richardson, Ph.D., and on behalf of the 315 Study Group

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that donepezil provides significant treatment benefits in cognition and global function in patients with severe Alzheimer's disease.

Summary:

Objective: To determine the efficacy and tolerability of donepezil in the treatment of patients with severe Alzheimer's disease (AD).

Method: Patients with severe AD (Mini-Mental State Examination [MMSE] scores, 1-12; Modified Hachinski Ischemic [MHI] scores, ≤6; and Functional Assessment and Staging [FAST] scores ≥6) were enrolled in this double-blind, placebo-controlled trial at 98 sites in Australia, Canada, France, the UK, and the US. Patients were randomized to 10 mg/d donepezil (after 5 mg/d for 6 weeks) or placebo for 24 weeks. The primary endpoints were change from baseline in Severe Impairment Battery [SIB] total score and Clinician's Interview-Based Impression of Change-Plus (CIBIC-Plus) at 24 weeks. Adverse events (AEs) were recorded throughout the trial. Statistical analyses on the intent-to-treat-last observation carried forward (ITT-LOCF) population included ANCOVA and CMH chi-square. CIBIC-Plus analysis assumed minimum values of 5 per category. If unmet, categories were collapsed (1-3=improved; 4=no change; 5-7=worsened). The CIBIC-Plus was also analyzed as a continuous variable.

Results: In total, 343 patients were randomized to donepezil (n=176) or placebo (n=167). Baseline characteristics at screening were similar between groups; mean [±SD] MMSE 7.5±3.38, MHI 0.8±0.97, and >55% with FAST ≥6c. Donepezil was significantly superior to placebo on the SIB score at endpoint (ITT-LOCF LS mean difference 5.32; P=.0001) and at Weeks 8, 16, and 24 (P<.0011). CIBIC-Plus using collapsed categories significantly favored donepezil for the ITT-LOCF (P=.0473) and at Week 24 (P=.0409). Analyzed as a continuous variable, the mean CIBIC-Plus score statistically favored donepezil at endpoint (P=.0168) and at Week 24 (P=.0323) in the ITT population. Most AEs were mild or moderate. The most common AEs reported were diarrhea, insomnia, nausea, headache, infection, and urinary incontinence.

Conclusion: Donepezil treatment in patients with severe AD resulted in greater efficacy on measures of cognition (SIB) and global function (CIBIC-Plus) compared with patients receiving placebo.

References:

1. Feldman H, Gauthier S, Hecker J, Vellas B, Subbiah P, Whalen E. A 24-week, randomized, double-blind study of donepezil in moderate to severe Alzheimer's disease. Neurology. 2001;57:613-620.

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NR887 Thursday, May 25, 12:00 PM - 2:00 PM

Psychological Assessment of HIV-Infected Patients Candidates for Liver Transplantation

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the most important aspects of a correct psychological assessment of HIV / HCV co-infected patients who want to be candidates for a orthotopic liver transplantation.

Summary:

Background: Liver transplantation (LT) is increasingly indicated in HIV-infected patients. The evaluation of these patients as LT candidates requires specific assessment of several psychological aspects, which may represent additional and unexpected difficulties.

Objective: To assess psychological aspects in HIV-infected patients under evaluation as LT candidates.

Methods: We evaluated 19 HIV-infected patients (17 males; mean age: 41 years) from the psychological point of view during their general evaluation as LT candidates. HIV infection was acquired through iv drug addiction in 13 patients, sexual contact in 2, and unknown route in 4.

Results: The attitude in front of the psychological evaluation was sincere in only 2 patients, passive in 11 and defensive-negative in 6. Thirteen patients had past history of alcohol abuse, although only 7 were conscious of it. In other 4 patients, alcohol abuse was unclear because of their little cooperation. Other drugs consumed by the patients were heroin (n=13), cannabis (n=16), cocaine (n=10) and benzodiazepines (n=19; abuse in 9). There was social-familiar disarrangement in 11 patients, and history of psychopathology in 15, probable personality disorders in 12, neuropsychological disorders in 7 and imprisonment in 2. Three patients were rejected for LT due to psychological reasons.

Conclusions: High prevalence of multiple drug abuse, psychopathology and social-familiar disarrangement can be often observed in HIV-infected patients who are candidates for LT. The little awareness of drug problems and the frequently insincere attitude of patients require an exhaustive psychological evaluation due to the possibility of occultation of information essential for their assessment as LT candidates.

References:

1. O'Grady J, Taylor C, Brook G.Guidelines for liver transplantation in patients with HIV infection. HIV Med. 2005 Jul;6 Suppl 2:149-53.

2. Moreno S, Fortun J, Quereda C, Moreno A, Perez-Elias MJ, Martin-Davila P, de Vicente E, Barcena R, Quijano Y, Garcia M, Nuno J, Martinez A. Liver transplantation in HIV-infected recipients. Liver Transpl. 2005 Jan;11(1):76-81.

NR888 Thursday, May 25, 12:00 PM - 2:00 PM

Psychiatric Morbidity and Impact on Hospital Length of Stay Among Hematologic Cancer Patients Receiving Stem-Cell Transplantation

Jordi Blanch, Ph.D. *Hospital Clinic, Psychiatry Department. Clinical Institute of Neurosciences, Villarreol 170, Barcelona, 08036, Spain*, Jesus Prieto, M.D., Jorge Atala, M.D., Enric Carreras, Ph.D., Montse Rovira, Ph.D., Esteve Cirera, M.D., Cristobal Gasto

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the prevalence of psychiatric disorders during hospitalization for hematopoietic stem-cell transplantation (SCT) and to get to know the impact of psychiatric disorders on hospital length of stay (LOS).

Summary:

Objectives: To determine the prevalence of psychiatric disorders during hospitalization for hematopoietic stem-cell transplantation (SCT) and to estimate their impact on hospital length of stay (LOS).

Patients and Methods: In a prospective inpatient study conducted from July 1994 to August 1997, 220 patients aged 16 to 65 years received SCT for hematologic cancer at a single institution. Patients received a psychiatric assessment at hospital admission and weekly during hospitalization until discharge or death, yielding a total of 1,062 psychiatric interviews performed. Psychiatric disorders were determined on the basis of the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition.* Univariate and multivariate linear regression analyses were used to identify variables associated with LOS.

Results: Overall psychiatric disorder prevalence was 44.1%; an adjustment disorder was diagnosed in 22.7% of patients, a mood disorder in 14.1%, an anxiety disorder in 8.2%, and delirium in 7.3%. After adjusting for admission and in-hospital risk factors, diagnosis of any mood, anxiety, or adjustment disorder ($P < 0.022$), chronic myelogenous leukemia ($P < 0.003$), Karnofsky performance score less than 90 at hospital admission ($P < 0.025$), and higher regimen-related toxicity ($P < 0.001$) were associated with a longer LOS.

Acute lymphoblastic leukemia ($P < 0.01$), non-Hodgkin's lymphoma ($P < 0.04$), use of peripheral-blood stem cells ($P < 0.001$), second year of study ($P < 0.001$), and third year of study ($P < 0.001$) were associated with a shorter LOS.

Conclusion: Our data indicate high psychiatric morbidity and an association with longer LOS, underscoring the need for early recognition and effective treatment.

References:

1. Prieto JM, Blanch J, Atala J, Carreras E, Rovira M, Cirera E, Gasto C. Psychiatric morbidity and impact on hospital length of stay among hematologic cancer patients receiving stem-cell transplantation. J Clin Oncol. 2002 Apr 1;20(7):1907-17.

2. Ickovics JR, Hamburger ME, Vlahov D, Schoenbaum EE, Schuman P. Mortality, CD4 cell count decline, and depressive symptoms among HIV-seropositive women: Longitudinal analysis from the HIV Epidemiology Research Study. JAMA 2001; 285:1466-1474.

NR889 Thursday, May 25, 12:00 PM - 2:00 PM

Depression Predicts Mortality Among Cancer Patients After Stem-Cell Transplantation

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to know the association between depression and survival among cancer patients

Summary:

Objective: To determine the association between depression and survival among cancer patients at 1, 3, and 5 years after stem-cell transplantation (SCT).

Patients and Methods: This was a prospective cohort study of 199 hematologic cancer patients who survived longer than 90 days after SCT and who were recruited in a University-based hospital between July 1994 and August 1997. Patients received a psychiatric assessment at four consecutive time points during hospitalization for SCT, yielding a total of 781 interviews. Depression diagnoses were determined on the basis of the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition.

Results: Eighteen (9.0%) and 17 patients (8.5%) met criteria for major and minor depression, respectively. Multivariate Cox regression models found major depression to be predictive of higher 1-year (hazard ratio [HR], 2.59; 95% CI, 1.21 to 5.53; P = .014) and 3-year mortality (HR, 2.04; 95% CI, 1.03 to 4.02; P = .041) but not 5-year mortality (HR, 1.48; 95% CI, 0.76 to 2.87; P = .249). Minor depression had no effect on any mortality outcome. Other multivariate significant predictors of higher mortality were higher regimen toxicity in the 1-, 3-, and 5-year models; older age and acute lymphoblastic leukemia in the 3- and 5-year models; chronic myelogenous leukemia in the 3-year model; and lower functional status and intermediate/higher risk status in the 5-year model. Use of peripheral-blood stem cells predicted lower mortality in the 5-year model.

Conclusion: After adjusting for multiple factors, major depression predicted higher 1- and 3-year mortality among cancer patients after SCT, underscoring the importance of adequate diagnosis and treatment of major depression.

References:

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2. Prieto JM, Blanch J, Atala J, Carreras E, Rovira M, Cirera E, Gasto C. Psychiatric morbidity and impact on hospital length of stay among hematologic cancer patients receiving stem-cell transplantation. J Clin Oncol. 2002 Apr 1;20(7):1907-1917.

NR890 Thursday, May 25, 12:00 PM - 2:00 PM

Safety and Tolerability of Rapid Versus Conventional Dose Escalation With Quetiapine in Acute Schizophrenia and Schizoaffective Disorder: A Randomized Multi-Center, Parallel, Group Open Trial

Giuseppina Boidi, Sr. *Asl 3 Genova-Italy, Mental Health, Genova, 16100, Italy*

Educational Objectives:

Educational objective: At the conclusion of this presentation, the participants should be able to describe the benefits associated with rapidly initiating quetiapine.

Summary:

Objective: Quetiapine is efficacious in acute psychosis and acute mania.[1-3] This study examined rapid dose escalation of quetiapine in acutely ill patients.

Methods: 2-week, multicenter, open trial of 269 inpatients diagnosed with schizophrenia (51%) or schizoaffective disorder (49%) randomized to rapid [Days 1-4: 200, 400, 600, 800mg] versus conventional [Days 1-4: 50, 100, 200, 300mg] dose escalation, followed by flexible dosing (maximum 800mg/day). Primary endpoint was patients experiencing ≥1 episode of any selected AE (somnolence, dizziness, orthostatic hypotension) during Week 1.

Results: The proportion of patients with >1 selected AE during Week 1 was 9.4% and 5.4%, and the most common AEs (>5%),

were hypotension (10.8%, 5.4%), tachycardia (7.9%, 5.4%), somnolence (5.8%, 2.3%) and sedation (4.3%, 3.1%), in the rapid and conventional groups, respectively. During Week 1, 3 (2.1%) patients from the rapid and 5 (3.8%) from the conventional group withdrew due to AEs. BPRS and CGI-S scores decreased significantly ($p<0.0001$) from baseline at Days 5 (BPRS changes: -15.91, -13.47; CGI-S changes: -4.27, -4.16) and 14 (BPRS changes: -26.47, -24.71; CGI-S changes: -3.53, -3.33) in the rapid and conventional groups, respectively.

Conclusion: Rapid dose escalation of quetiapine to 800mg/day by Day 4 appears effective, generally safe and well tolerated in this population.

Funding sources: AstraZeneca Pharmaceuticals

References:

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2. Arango C. et all, Curr Med Res Opin 2004; 20: 619-626
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NR891 Thursday, May 25, 12:00 PM - 2:00 PM

Implementation of Recommendations Mmade During Pediatric Telepsychiatry Consultation: A Case Study

Katherine M. Boydell, Ph.D. *University of Toronto, Psychiatry, 555 University Avenue, Toronto, ON, M5G 1X8, Canada*, Natasha Greenberg, M.A., Tiziana Volpe, M.A.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to identify the facilitators and barriers to the implementation of recommendations made during a pediatric telespychiatry consultation.

Summary:

Although the use of technological media to deliver psychiatric services has become increasingly popular, very little rigorous research and review into the outcomes of health services delivered in this way has been undertaken. While published literature on client and provider satisfaction with telepsychiatry services exists, qualitative and quantitative considerations of other outcomes, such as cost-effectiveness, clinical, and program outcomes, are notably absent in the literature. In this study, a record review of one hundred randomly selected telepsychiatry consultations by a pediatric telepsychiatry consultation program serving rural and remote communities in Ontario was undertaken. This review was followed by in depth telephone interviews with case managers associated with these cases, in which the barriers and facilitators to successful program outcomes were further explored. Case managers acknowledged the expertise provided by the telepsychiatry program, and noted the respect afforded this expertise in their communities in general. They indicated that the participation of key stakeholders in the consultation process increases the willingness to try new treatments, treatment adherence, and continuity of care across the various contexts of children's daily lives.

References:

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NR892 Thursday, May 25, 12:00 PM - 2:00 PM

Crack/Cocaine Use Among Adolescents and HIV-Associated Risk

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to 1) identify the risks associated with crack/cocaine use among adolescents and 2) estimate the prevalence of crack/cocaine use among adolescents with psychiatric disorders.

Summary:

Introduction: Crack/cocaine use among adults has been associated with other psychiatric disorders and a wide variety of risk behaviors such as other drug use and unprotected sex. The issue is relatively unstudied in adolescents, especially younger teens.

Methods: 310 adolescents from intensive treatment settings with a mean age of 14.5 years were assessed for drug use, risk behaviors and risk attitudes. The sample was 45% male, 87% white and exhibited a wide range of psychiatric disorders such as mood disorders (40%), impulse control disorders (29%), and anxiety disorders (9%). None had been admitted with a primary diagnosis of substance abuse.

Results: 13% of youth reported ever using crack or cocaine. Use was not associated with age, gender, race, SES, or psychiatric diagnosis (except for a greater proportion of substance abuse treatment). Use, compared to non-use, was significantly ($p< .01$) associated with elevated rates of risk behaviors such as daily alcohol use (38% versus 4%), daily marijuana use (49% versus 9%), frequent self-cutting (60% versus 19%), history of sexual activity (92% versus 67%), more than 2 sex partners in past year (41% versus 18%) and history of STD (14% versus 3%). A multiple logistic regression found that after controlling for factors that influence unprotected sex such as age, gender, race, history of sexual base and self-restraint attitudes, that those with a history of crack/cocaine were 12.6 times more likely to have engaged in unprotected sex than their peers.

Conclusions: Crack/cocaine use is prevalent even among younger adolescents with psychiatric disorders who are not in drug treatment. Its use is associated with high rates for sexual, drug and self-cutting risk behaviors. A history of use should alert clinicians to a wide variety of possible behavioral risks. Programs that target behavioral risk need to account for crack/cocaine use, even among younger teens.

References:

1. Ross MW, Hwang, L, Zack, C, et al: Sexual risk behaviours and STIs in drug abuse treatment populations whose drug of choice is crack cocaine. Int J STD AIDS 2002; 13:769-774.
2. Brown LK, Houck CD, Hadley WH, et al: Self-cutting and sexual risk among adolescents in intensive psychiatric treatment. Psychiatr Serv 2005; 56:216-218.

NR893 Thursday, May 25, 12:00 PM - 2:00 PM

Co-morbid Depression and Anxiety in Later Life: Patterns of Associations and Impairment

John Cairney, Ph.D. *University of Toronto, 33 Russell Street, Toronto, ON, M5S 251, Canada*, Scott Veldhuizen, B.A., Laurie

M. Corna, M.S.C., David L. Streiner, Ph.D., Laura McCabe, M.D., Nathan Hermann, M.D.

Educational Objectives:

At the conclusion of this presentation, participants will better understand the patterns of psychiatric co-morbidity and impairment in a community-based sample of Canadian adults aged 55 and older, as well as the implications of these findings for integrated care in this population.

Summary:

Objective: Until recently, most large epidemiologic surveys of mental disorder have excluded older adults. Gaps therefore exist in our understanding of the epidemiology of psychiatric disorder in later life. In this study, we examine psychiatric co-morbidity and impairment in a community-based sample of adults aged 55 and older.

Method: Analysis of a large sample of older adults (n=12,792) from a representative Canadian survey conducted in 2002. The WMH-CIDI is used to diagnose 12-month DSM-IV major depression (MD), panic disorder (PD), social phobia (SP), and agoraphobia (AP).

Results: All four disorders are less prevalent among older adults, with 4.6% (95%CI=3.9-5.2) having one or more compared to 9.4% (95%CI=8.9-9.9) among those 15-54. Comorbidity is common, however, with 18% (95%CI=12.6-23.5) of those with any disorder having at least one other. Bivariate associations are strongest between MD and SP (phi correlation = 0.22, $p<0.001$) and between MD and PD (phi r = 0.2, $p<0.001$). Older adults with both MD and an anxiety disorder (n=66) report the worst physical health and the greatest impairment of any group. Independent associations with specific physical conditions are weaker than among younger adults, with only migraine headaches predicting comorbidity (OR= 4.9, 95%CI=2.0-11.9, $p<0.001$).

Conclusions: While co-morbid physical health and depression, and dementias and depression are well documented, these results support work indicating that co-morbid depression and anxiety is also prevalent in later life. Comorbidity is associated with high levels of impairment, and, though a minority in the community, comorbid cases are likely to be very common in clinical settings. Poor physical health in this group underlines the need for integrated care, and, given demonstrated links between physical and mental health, better recognition and treatment of comorbid conditions has the potential to improve overall health and quality of life.

References:

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2. Beekman AT, de Beurs E, van Balkom AJ et al. Anxiety and depression in later-life: Co-occurrence and communality of Risk Factors. American J Psychiatry 2000; 157: 89-95.

NR894 Thursday, May 25, 12:00 PM - 2:00 PM

Prevalence and Level of Recognition of Cardiovascular Risk Factors in Schizophrenia: The Spanish Ricava Study

Miquel Bernardo *Barcelona*, Fernando Canas de Paz, Jose Ramon Banegas, Jordi Casademont, Yolanda Riesgo, Cristina Varela

Educational Objectives:

Participants will have a better knowledge about cardiovascular risk factors prevalence and management among schizophrenic patients in a country on the Mediateranean Area.

Summary:

Objective: To estimate the prevalence and level of recognition of Cardiovascular Risk Factors (CVRF) in patients with schizophrenia in Spain (Mediteranean Area).

Methods: Cross-sectional multicenter descriptive study. Each risk factor was established according to international criteria and/ or therapeutic treatment.

Results: 733 evaluable patients (72% men, 38% women, average age 38 (SD 11.3)) from 97 acute units (61% of those in Spain) were studied. Prevalent CVRF (weighted by Constituent Communities population) were: smoking (71%), sedentarism (70%) hypercholesterolemia (66%), abdominal obesity (35%), hypertriglyceridemia (28%), hypertension (18%), hyperuricaemia (14%) and metabolic syndrome (19%). Most commonly identified risk factors where risk behaviors involving excessive alcohol intake (73%) and smoking (52%); most treated ones were hypertension (69%) and diabetes (41%).

Conclusions: Comorbid metabolic disorders in patients with schizophrenia are prevalent and underrecognized by health care professionals and patients. Thus, it is prudent for the psychiatric community to be aware of comorbid medical conditions other than risk behaviours.

References:

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2. ADA, American Psychiatric Association, American Association of Clinical Endocrinologists, North American Association for the Study of Obesity. Consensus development conference on antipsychotic drugs and obesity and diabetes. Diabetes Care 2004;27;2;5.

NR895 Thursday, May 25, 12:00 PM - 2:00 PM

Barriers to the Diagnosis of Catatonic Schizophrenia

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Educational Objectives:

At the end of this presentation the participant will be able to identify the barriers in terminology, definition and application. At the end of this presentation the participant will be able recognize the reasons why a new approach to DSM-V and ICD-10 classification of this disorder is warranted.

Summary:

The objective of this study was to identify barriers to the diagnosis of catatonic schizophrenia in the International Classification of Disease, 9th Revision, Clinical Modification (ICD-9-CM) and the Diagnostic and Statistical Manual for Mental Disorders, 4th Edition and Revised (DSM-IV and DSM-IV-TR) for diagnostic and coding issues related to catatonic schizophrenia. This has been a concern for the Catatonia Consortium, a freestanding department of clinicians and researchers in the field of motility psychoses. Methods: We reviewed the clinical barriers to diagnosis of catatonia identified in 3 books written on the subject. We also developed a 10-question test to detect comprehension of catatonic signs. Results: We found 13 separate clinical barriers to the diagnosis of the catatonic subtype. We found a lack of consensus among experts on the catatonia test among consortium members and low scores among a freestanding department of clinicians from other settings. Discussion: Our findings support the work of van der Heijden, et

al. who found that under 2% of patients were diagnosed with catatonia although 18% had 2 or more signs. We found barriers in terminology, definition and application that suggest that a new approach to DSM-V and ICD-10 classification of this disorder is warranted.

References:

1. Ungvari GS, Chow LY, Leung HCM, Lau BST. Rating chronic catatonia: discrepancy between cross-sectional and longitudinal assessment. Revista de Psiquiatria Clinica (Brazil), 1999; 26: 56-61.
2. van der Heijden FM, Tuinier S, Arts NJ, Hoogendoorn ML, Kahn RS, Verhoeven WM. Catatonia: disappeared or underdiagnosed? Psychopathology 2005; 38:3-8.

NR896 Thursday, May 25, 12:00 PM - 2:00 PM

The Neural Circuitry of Catatonia

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Educational Objectives:

The participant should be able to discuss the concept of schizophrenia with catatonic features. The participant should be able to recognize the major neural pathways involved in catatonia. The participant should be able to recognize the pharmacology involved in catatonia.

Summary:

Objective: To identify the neural circuitry that underlies catatonia. This neural circuit is important to establish to understand psychosis in other modalities (e.g. visual hallucinations) and other motility psychoses (e.g. autism). Methods: We reviewed the literature on the neuroscience and pharmacology of catatonia, including 2 books written on the subject. We also examined somatic treatments in a naturalistic study in one neuropsychiatry hospital. Results: We found 35 patients with schizophrenia with catatonic features (66% of those with catatonia). We have found that memantine 10 mg bid (adjunct) may help to reduce mutism, negativism, immobility and posturing (N=5). Adjunctive memantine did not improve positive symptoms (N=3) and seems to work only in catatonic features and not in disorganized, undifferentiated, and paranoid schizophrenia (N=2). This response was included into existing neuroscience models of catatonia. Discussion: Our findings support the neuronal circuitry of a motor loop including the frontal lobe, basal ganglia, amygdala, parietal lobe and supplemental motor area. The neurochemistry of catatonia appears to involve low activity within Gamma-aminobutyric acid, and dopamine systems with high activity within the glutamate (NMDA) system. The catatonia neural circuit illustrates a comprehensive neuroscience approach to the motility psychoses with prospects for prevention and treatment.

References:

1. Fink M, Taylor MA. Catatonia: A Clinician's Guide to Diagnosis and Treatment, Cambridge, UK, Cambridge University Press, 2003.
2. Caroff SN, Mann SC, Francis A, Fricchione GL (eds) Catatonia: From Psychopathology to Neurobiology. American Psychiatric Press, Washington, DC 2004.

NR897 Thursday, May 25, 12:00 PM - 2:00 PM

Listening Too Much to Kramer? A Critique of Cosmetic Psychopharmacology

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to demonstrate an understanding of the term cosmetic psychopharmacology (CP) and its relevance to psychiatry. The participant will learn the history of the CP, review the evidence that current psychiatric medicines are not forms of CP, and understand how critics of psychiatry on both the left and right continue to use the ambiguity involved in CP to cast doubt upon the treatment of depression and other forms of mental illness. Only by properly understanding this new challenge to psychiatry can we as a profession properly respond.

Summary:

The writings of Peter Kramer represent "conventional wisdom" with respect to what has come to be called "cosmetic psychopharmacology," or the use of pharmaceuticals to alter mood and temperament in those without mental illness. In his earlier and extremely popular book, *Listening to Fluoxetine*, Kramer worried that Fluoxetine was the first cosmetic psychopharmaceutical. Kramer agonized over whether to withhold this treatment from patients, fearing that Fluoxetine could change a patient's fundamental "self." In his new book, *Against Depression*, Kramer comes full circle (almost), and now agonizes over the withholding of effective antidepressant treatments from patients who might benefit from them (regardless of whether they meet the full DSM-IV criteria).

While I applaud Kramer's recent efforts to de-stigmatize depression and improve its treatment, it may be a question of "too little, too late." *Listening to Fluoxetine* fueled (and continues to fuel) the neo-antipsychiatry movement. Depression is once again being viewed as a side-effect of a weak constitution (lack of willpower) or as an issue of social morality (drug seeking for narcissistic reasons). This new movement is reflected in powerful voices like those of Leon Kass and the *President's Council on Bioethics* (on the right) and Carl Elliot and his supporters (on the left).

The major flaw in *Against Depression* is that it does not rectify Kramer's earlier incorrect notions that SSRI's are a form of cosmetic psychopharmacology. While Kramer points out that some of the "cosmetic" patients mentioned by Elliot and Kass may in fact have depression, he never critically examines his earlier work. The cases presented in *Listening to Fluoxetine* were clearly suffering from depression and anxiety and were often more severe than those cases presented in *Against Depression*. Yet Kramer never points out this fact and the obvious inference it implies: that his earlier fears about SSRI's and cosmetic psychopharmacology were misplaced.

Another major criticism of Kramer is that the conclusions in *Against Depression* can and should have been drawn a decade and a half ago when he wrote *Listening to Fluoxetine*. There have been no major paradigm shifts in the neuroscience of depression and its treatment: in 1993, it was considered a brain disease (discussed in terms of neurotramsmitters and endocrine function); in 2005, it is still considered a brain disease (discussed in terms of neurotransmitters, endocrine function, and neural networks). As Kramer himself acknowledges, *Listening to Fluoxetine* thrust him into the spotlight of depression and he began to specialize in the treatment of refractory depression. This experience led him to question some of his earlier psychoanalytical views of psychiatry and adopt a more biological approach, yet Kramer fails to appropriately criticize his earlier arguments.

While I think *Against Depression* is a helpful and accurate book in the fight against depression, it does not correct Kramer's earlier mistakes. Only by admitting his earlier Extended Release rors and challenging the powerful neo-antipsychiatry movement directly can Kramer hope to reverse the stigma he has helped to create around the very disease he now battles so vigorously to defeat.

References:

1. Kramer, PD: Against Depression. New York, NY, Viking, 2005.
2. Elliot C, Chambers T (Eds).: Prozac As a Way of Life. Chapel Hill, NC, The University of North Carolina Press, 2004.

NR898 Thursday, May 25, 12:00 PM - 2:00 PM

A Paranoid Spectrum Hypothesis Based on Cognitive and Clinical Comparisons Between Delusional Disorder and Schizophrenia Patients

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize:

1) The existence of empirical evidence supporting the theory of a paranoid dimension expressed in a continuum fashion accross different psychotic disorders.

2) Constructual inconsistencies in currently accepted psychotic categories.

3) The importance of a dimensional approach in the understanding of psychoses

4) The need for searching more valid psychotic phenotypes.

Summary:

Introduction

Conceptual inconsistencies in current diagnostic categories of psychoses may account for frequent failures to replicate neurobiological correlates of schizophrenia. This could herald an inadequate construct validity of currently accepted psychotic phenotypes. In particular, Paranoid Schizophrenia (PS), yet included within the same nosological category than Non-Paranoid Schizophrenia (NPS), may plausibly constitute a different disorder sharing some characteristicst to Delusional Disorder (DD).

Methods: 102 patients fulfilling DSM-IV-TR criteria of schizophrenia (56 PS and 46 with NPS) and 80 DD patients were included in this study **(n=182)**. All patients were recruited from a psychotic disorders case register available from a computerized medical records software facility at public mental health service out-patient units in Barcelona, Spain. Diagnostic status was established using the SCID to get patients assigned to either DD, PS or NPS groups. A battery of psychopathological (PANSS) and neuropsychological tests (MMSE, TMT, CPT, WCST, Stroop, FAS and selected WAIS subtests) were administered. We performed multinomial regression to compare psychopathological and neuropsychological findings accross the three psychotic categories (DD versus PS versus NPS) adjusting for age, sex, education years, global functioning (GAF) and years with the disorder.

Results

Patients with DD tended significantly to be more frequently female and married than those with PS or NPS. We found associations between negative (DD Base;PS:OR=26(CI:24-28)p=0.004;NPS:OR=43(CI: 39-47)p=0.003), paranoid (DD Base;PS:OR=0.26(CI:.01-.4)p=.011;NPS:OR= 0.02(CI: .01-36)p=.008), affective and hostile symptom dimensions (extracted by PCA using all PANSS items) and outcome. Associations exhibited either linear tendency along the three types of psychosis or halfway position for PS compared to DD and NPS. Most cognitive tests also showed significant associations in the predicted direction (PS showing intermediate performance between DD and NPS), including global functioning, attention, verbal fluency, working and semantic memory tests.

Conclusions

Findings support the hypothesis suggesting a continuum of paranoidsm and cognitive impairment accross the studied psychotic groups.

References:

1. Liddle, P. Disordered Mind and Brain: The neural basis of mental symptoms. London, Gaskell, 2001.
2. Bentall, R. Madness Explained: Psychosis and Human Nature. London, Penguin Psychology, 2003.

NR899 Thursday, May 25, 12:00 PM - 2:00 PM

Unexplained Medical Symptoms in Multiple Organ Systems and Adverse Childhood Experiences

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Educational Objectives:

To recognize the association between ACEs and UMS involving multiple organ systems and describe the clinical implications of this association.

Summary:

Objectives: Patients with unexplained medical symptoms (UMS) involving multiple organ systems pose diagnostic and treatment challenges for physicians. Although these patients may be suffering from hypochondriacal, somatization, or conversion disorders, the role that adverse childhood experiences (ACEs) may assume in UMS involving multiple organ systems has not been previously investigated. Methods: Data were from the ACE Study, a retrospective cohort investigation of HMO patients receiving biopsychosocial evaluations (N=17,337). Patients were assigned an ACE score comprised of the number of eight categories of childhood abuse or household dysfunction they reported. UMS were defined using a review of systems, with no corresponding diagnosis in the patient's medical record. Symptoms across five systems (respiratory, gastrointestinal, CNS, cardiovascular, and musculoskeletal) were assessed, as were the number of physician office visits. Results: ACE scores were positively associated with the number of organ systems involved in UMS ($p<.001$), the total number of UMS ($p<.001$), and the mean number of doctor visits in the previous year ($p<.001$). Discussion: These results suggest assessment for ACEs may promote earlier evaluation of UMS across multiple organ systems, which may underlie increased healthcare utilization.

References:

1. Chapman DP, Perry GS, Strine TW. The vital link between chronic disease and depressive disorders. Prev Chronic Dis 2005: 2:1-10.
2. Walker EA, Unutzer J, Katon WJ. Understanding and caring for the distressed patient with multiple medically unexplained symptoms. J Am Board Fam Pract 1998;11:347-356.

NR900 Thursday, May 25, 12:00 PM - 2:00 PM

Paranoia in Social Phobia

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Educational Objectives:

At the conclusion of this presentation the participant should have a better understanding of the incidence of paranoid personality traits in anxious depressives.

Summary:

Objective: Social Phobia (SPh) is one of the most prevalent anxiety disorders. It is a persistent and debilitating condition strongly associated with significant academic and occupational disability, poorer quality of life and overuse of substances. Diagnosing a co-occurring personality disorder in patients with an axis I disorder is clinically important because of their association with the duration, recurrence, and outcome of axis I disorders. High co-occurrence of avoidant personality disorder and SPh is a common finding in research studies and clinical offices. Limited data exists regarding paranoid personality (PPD) traits in SPh, which are commonly encountered by therapists treating socially anxious individuals. In this exploratory study we examined prevalence of PPD and paranoid traits in patients presenting with various anxiety disorders (ADs). **Method:** As a part of the MIDAS project, 1700 outpatients were evaluated with the SCID and SIDP. To control for the frequent elevation of axis II pathology in depression and its high comorbidity with ADs, to address the question of whether paranoid personality traits are more strongly associated with SPh than with other ADs we selected for our analyses depressed patients only. The prevalence of PPD and the total scores of the PPD dimension were compared in 3 nonoverlapping depressive groups: 1)no ADs (n=284), 2)some ADs but no SPh (n=266), 3)SPh with or without other ADs (n=308). **Results:** The prevalence of PPD was significantly higher in group 3 than groups 1 and 2 (8.8% versus 2.1% and 5.3%). Similar results were obtained for the total score of the paranoia dimension (3.3 versus 1.5 and 2.6). **Conclusions:** Given the facets of the PPD, such as suspiciousness, hypersensitivity, and extreme vigilance it is not surprising that this PD and its traits showed stronger association with SPh than with other anxiety disorders, even when controlling for depression.

References:

1. Wittchen H, Fehm L: Epidemiology and natural course of social fears and social phobia. Acta Psychiatrica Scandinavica 2003; Sup 417,108:4-15.

2. Van Velzen C, Emmelkamp P, Scholing A: Inconveniences and characteristics of personality in a sample of subjects of social phobia. Psicologia Conductual Revista 2003; 11:527-537.

NR901 Thursday, May 25, 12:00 PM - 2:00 PM

Korean Version of the Montreal Cognitive Assessment: A Brief, Mild Cognitive Impairment Screening Tool in an Illiterate Person

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize reliability of the Korean version of the Montreal Cognitive Assessment for minimal cognitive impairment screening.

Summary:

Backgrounds: Montreal Cognitive Assessment (MoCA) is a brief cognitive screening tool with high sensitivity (90%) for detecting Mild Cognitive Impairment (MCI) in literated person. But, in developing countries like Korea, a lot of elderly people are illiterate and MoCA can not be used without modification.

Objectives: To modify a 10-minute cognitive screening tool (MoCA) to detect mild cognitive impairment in literate and illiterate elderly people.

Methods:

To validate Korean version of the Montreal Cognitive Assessment (MoCA-K), MOCA-K, Korean version of Mini-Mental State Examination (MMSE-KC) and neuropsychological batteries were administered to one hundreds elderly persons (mild Alzheimer's disease (AD)=25, MCI=25, Normal controls (NC)=50) who are illiterate persons.

Results:

MMSE-KC had a sensitivity of 10% to detect MCI. MoCA-K had a sensitivity of 85% to detect MCI. In the mild AD group, MoCA-K had a sensitivity of 100% to detect AD.

Specificity was high in MoCA-K.

Conclusions:

MCI was understood as preclinical stages of AD. The MoCA-K is a good brief cognitive screening tool with high sensitivity and specificity for detecting MCI in illiterate elderly persons.

References:

1. Nasreddine ZS et al.: The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. J Am Geriatr Soc. 2005; 53:695-659.

2. Nordlund A et al.: The Goteborg MCI study: mild cognitive impairment is a heterogeneous condition. J Neurol Neurosurg Psychiatry. 2005; 76:1485-1490.

NR902 Thursday, May 25, 12:00 PM - 2:00 PM

Predictors of Quality of Life in Alzheimer's Dementia Patients in Korea

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the factors affecting quality of life among Korean dementia patients.

Summary:

Objectives : The aim of this study was to analyze factors affecting quality of life (QOL) among Korean dementia patients.

Methods : The subjects were consisted with 54 patients with dementia of the Alzheimer's type and 54 normal aged controls with age over 60. The QOLs were assessed with the Korean Version of the Quality of Life in Alzheimer's Disease: Patient and Caregiver Report (KQOL-AD). For analyzing factors affecting QOL in dementia, the clinical data were obtained by structured interview and medical records, serum homocysteine levels were measured, and the severity of dementia (Mini-Mental State Examination, Clinical Dementia Rating, Global Deterioration Scale), functional activities (Activities of Daily Living, Instrumental Activities of Daily Living) and depression (Geriatric Depression Scale) were evaluated using various rating scales.

Results : 1) The mean (±S.D.) score of KQOL-AD in patients with dementia of the Alzheimer's type (24.30 ± 5.06) was significantly ($p<0.005$) lower than those in normal aged controls (26.56 ± 3.25).

2) The factors influencing on KQOL-AD in patients with dementia of the Alzheimer's type were age ($p<0.01$), cognitive function ($p<0.01$), severity of dementia ($p<0.01$), activities of daily living

($p<0.01$), depression ($p<0.01$) and serum homocysteine levels ($p<0.05$).

Conclusion : In conclusion, multiple factors including problems originated from dementia itself as well as causes fundamentally related with pathophysiology of demenita might influence on the quality of life in patients with the Alzheimer's dementia.

References:

1. Ready RE, Ott BR, Grace J: Patient versus informant perspectives of Quality of Life in Mild Cognitive Impairment and Alzheimer's disease. Int J Geriatr Psychiatry 2004; 19(3):256-65.
2. Mintzer JE: What are the challenges faced by psychiatrists in the management of Alzheimer's disease? CNS Spectr 2004; 9(7 Suppl 5):13-5.

NR903 Thursday, May 25, 12:00 PM - 2:00 PM

West Nile Virus and Conversion Disorder: Case Report

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the possible clinical presentations of West Nile Virus and the potential of misdiagnosing West Nile Virus as conversion disorder.

Summary:

West Nile Virus (WNV) has spread across the country since its introduction to the United States in 1999. In severe cases, WNV can be complicated by a number of neurological deficits, thus possibly mimicking conversion disorder. Here we report a 19-year-old pregnant female referred to psychiatry as a possible case of conversion disorder who later tested positive for West Nile Virus.

Case Report

Ms. A, a single, 19-year-old African American woman, was admitted to the obstetrics and gynecology unit of a teaching hospital in her eighth month of pregnancy after presenting with unilateral paralysis of her right leg and foot. A routine examination including a complete blood count, electrolytes, urea, liver and thyroid function tests, urinalysis, and a non-contrast CT scan of the head yielded normal results. An initial diagnosis of a neurological deficit secondary to compression of the sciatic nerve was made; however, repeated maneuvering of her posture as well as a neurology consult did not indicate involvement of the sciatic nerve. A psychiatric consult was called to rule out conversion disorder.

The fact that Ms. A did not have any current or previous stressors and the fact that she was psychiatrically asymptomatic argued against a diagnosis of conversion disorder. We therefore recommended to the primary treatment team to investigate Ms. A more aggressively. Following further testing, Ms. A was positively confirmed for West Nile Virus infection.

This case demonstrates that patients infected with WNV can present with neurological deficits without any other symptoms associated with WNV, and thus mimic conversion disorder. Psychiatrists, family physicians, and internists should be aware that WNV has increased in prevalence over recent years and may be mistaken for a psychiatric diagnosis such as conversion disorder.

References:

1. Saad M, et al: Acute flaccid paralysis: the spectrum of a newly recognized complication of West Nile Virus Infection. J Infect 2005; 51:120-7.
2. Campbell GL, Marfin AA, Lanciotti RS, Gubler DJ: West Nile virus. Lancet Infect Dis 2002; 2:519-29.

NR904 Thursday, May 25, 12:00 PM - 2:00 PM

Cerebral Blood Flow Changes During Vagus Nerve Stimulation for Depression

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to:

1. Better understand the regional brain effects of acute vagus nerve stimulation in individuals with treatment-resistant depression.
2. Attempt to correlate the regions undergoing acute increased/decreased blood flow

with our current understanding of the central nervous system pathways of the vagus nerve.

3. Begin to draw some initial/preliminary conclusions regarding the regions undergoing acute activation and existing knowledge of regional brain involvement in mood disorders (especially treatment-resistant depression).

Summary:

Objective: To identify changes in rCBF in response to acute vagus nerve stimulation (VNS) in subjects with treatment resistant depression (TRD). [15O]H2O PET was used to detect brain regions of increased and decreased regional CBF (rCBF) in response to acute VNS stimulation.

Method: Four TRD subjects were enrolled. Prior to sustained VNS, they received 90-second [15O]H2O PET scans in an off-on sequence, (two scans with VNS de-activated and two with VNS activated), to coincide with an intravenous bolus injection of 50 mCi of [15O]H2O. PET images were aligned, normalized for global uptake, and resampled to standard atlas space. Statistical t-images were then calculated to evaluate VNS-induced changes (to determine regions demonstrating greater or less rCBF as a result of acute VNS activation). Additionally, HRSD24 scores were obtained at baseline, 3, and 9 months VNS.

Results: Statistically significant, VNS-induced increases in rCBF were found in 12 regions and decreases in 9 regions. Key regions undergoing increased rCBF included: inferior frontal gyrus, posterior orbital gyrus, medial orbital gyrus, anterior cingulate, anterior insula, putamen, superior frontal gyrus, cerebellar body, fusiform gyrus and precentral gyrus. Areas that underwent decreased rCBF included: inferior parietal lobule, superior parietal lobule, inferior temporal gyrus, medial temporal gyrus, post central gyrus, precentral gyrus, and the precuneus. The mean percentage change in HRSD24 scores from baseline was 65.2% after three months of VNS therapy and 39.6% after 9 months.

Conclusions: Acute VNS in TRD subjects caused significant rCBF changes in specific brain regions (orbitofrontal cortex, insula, anterior cingulate cortex, superior and middle frontal cortex, anterior temporal lobe) previously identified with metabolic abnormalities in mood disorders. These regions are part of the "upstream" vagus afferent pathway and have consistently demonstrated abnormal activity in previous neuroimaging studies of depression.

References:

1. Henry TR, Bakay RA, Votaw JR, et al.: Brain blood flow alterations induced by therapeutic vagus nerve stimulation in partial epilepsy: I. Acute effects at high and low levels of stimulation. Epilepsia 1998a; 39(9):983-990.

2. Mayberg HS: Modulating dysfunctional limbic-cortical circuits in depression: towards a development of brain-based algorithms for diagnosis and optimised treatment. Br Med Bull 2003; 65:193-207.

NR905 Thursday, May 25, 12:00 PM - 2:00 PM

Subacute and Chronic Brain Metabolic Change With Vagus Nerve Stimulation in Depression

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Educational Objectives:

1. To better understand the subacute and chronic metabolic brain changes occurring as a result of sustained vagus nerve stimulation in individuals with treatment resistant depression.
2. To begin to understand the chronology of these "evolving" brain metabolic changes and the correlation that these changes have with antidepressant treatment outcomes.
3. To begin to understand the potential mechanism of action of the recently Food and Drug Administration (FDA)-approved treatment for depression, Vagus Nerve Stimulation.

Summary:

Objective: To determine the metabolic effects of sustained vagus nerve stimulation (VNS) in treatment resistant depression (TRD).

Methods: 7 TRD subjects entered the study and underwent *Fluorodeoxyglucose (FDG)* PET scans at baseline (prior to VNS) and 3 months VNS. Four subjects were subsequently scanned at 24 months. All received baseline FDG PET scans immediately prior to implantation. Subjects received IV injection of 0.07 mCi/kg FDG and imaged after 45 minutes of FDG uptake using a General Electric Advance PET scanning system using 3-dimensional mode acquisition for 10 minutes. Images were reconstructed using a calculation attenuation factor. Images were summed and mean differences from baseline (using a t-score threshold of 3.5) determined.

Results: Subacute metabolic changes occurring at 3 months of stimulation are markedly different, both in direction (more deactivation at 24 months than 3 months) and degree (greater deactivation at 24 months). An "evolving" pattern of change with added duration of stimulation was observed. *Areas of activation/deactivation noted at 3 months* include: right thalamus (activation), and bilateral inferior temporal gyrus and fusiform gyrus, bilateral medial orbital gyrus, and left gyrus rectus (deactivation). *Following 24 months of active VNS*, activations were observed for left temporal gyrus, left anterior insula, right anterior insula, left cingulate gyrus, and right medial orbital gyrus. Deactivations were noted in the right parietal lobule, right medial frontal gyrus, left medial frontal gyrus, left inferior frontal gyrus, and left medial orbital gyrus.*Conclusions*: Subacute and chronic VNS causes different patterns of metabolic change consistent with "evolving" brain change. Summed average regional differences in activation/deactivation occurred in regions previously identified as along the pathway of the vagus nerve and have been demonstrated to be involved in mood disorder treatment responses by other treatment modalities (egs., ECT, pharmacotherapy).

References:

1. Rush AJ, Sackeim HA, Marangell LB, et al.: Effects of 12 Months of Vagus Nerve Stimulation in Treatment Resistant Depression: A naturalistic study. Biol Psychiatry 2005b;58:354-363.
2. Mayberg HS, Brannan SK, Tekell JL, et al.: Regional metabolic effects of fluoxetine in major depression: serial changes and relationship to clinical response. Biol Psychiatry 2000;48(8):830-843.

NR906 Thursday, May 25, 12:00 PM - 2:00 PM

The Epidemiology of Panic Disorder in Later Life: Results From a Large, National Survey of Canadians

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Educational Objectives:

At the conclusion of this presentation, participants will better understand the epidemiology of panic disorder, including its associated risk factors, among adults aged 55 years and older.

Summary:

Objective: Anxiety disorders, including Panic Disorder, are among the most common psychiatric disorders in older populations. However, compared to younger adults, much less is known about the epidemiology of the disorder, including associated risk factors, among older adults. This study examines the prevalence, risk factors, and co-morbidity of panic disorder in community dwelling older adults.

Method: The data come from the Canadian Community Health Survey (1.2), which is a nationally representative sample of community dwelling Canadians. Our sample includes adults aged 55 years and older (N=12,792). In multivariate models we investigate demographic and socio-economic variables as predictors of panic disorder, as well as the association of panic disorder with other mental disorders and physical health problems.

Results: The 12-month and lifetime prevalence estimates of panic disorder in this sample are 0.81% and 2.40% respectively and one fifth of these cases report a first onset after the age of 55 years. In multivariate models, the risk of panic disorder decreases with older age (OR=0.94, 95% CI=0.90-0.97) and is higher in the lowest-income group (OR=3.16, 95% CI=1.7-5.8). Physical limitations in daily activities as well as the presence of other psychiatric disorders (major depression, social phobia and mania) were also significantly associated with panic disorder in this sample.

Conclusions: Consistent with previous research on panic disorder, the prevalence of the disorder decreases with age among older adults. Our lifetime estimate is slightly higher than the lifetime estimate from the National Co-Morbidity Replication Study for adults 60 years and older, however, the 12-month estimate is fairly consistent with European estimates. The clinical implications of the physical and mental health co- morbidities with panic disorder, as well as the associated socio-demographic risk factors in this population are discussed.

References:

1. Sheikh JI, Swales PJ, Carlson EB, Lindley SE: Age and Panic Disorder Phenomenology, Comorbidity, and Risk Factors. Am J Geriatr Psychiatry 2004; 12:102-109.
2. Birchall H, Brandon S, Taub N: Panic in a general practice population: prevalence, psychiatric comorbidity and associated disability. Soc Psychiatry Psychiatr Epidemiol 2000; 35:235-241.

NR907 Thursday, May 25, 12:00 PM - 2:00 PM

The Effect of Memantine on Distinct Behavior Syndromes in Moderate to Severe Attention Deficit Patients

Jeffrey L. Cummings, M.D. *UCLA Alzheimer's Disease Center, 710 Westwood Plaza, Ste. 2238, Los Angeles, CA, 90095,* Jason T. Olin, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the potential for memantine to provide specific benefits to AD patients for mood- and psychosis-related behavioral symptoms based on the Neuropsychiatric Inventory.

Summary:

Objective: In a previously reported 24-week placebo-controlled, double-blind clinical trial in moderate-to-severe AD patients on concomitant donepezil treatment, memantine-treated patients performed significantly better on the Neuropsychiatric Index (NPI) than placebo-treated patients. The current study is a post hoc analysis in which NPI individual items were aggregated into four subscales to determine whether memantine has specific effects on one or more subscales. Memantine is a moderate affinity, uncompetitive N-methyl-D-aspartate (NMDA) receptor antagonist approved in the U.S. and Europe for moderate-to-severe AD.

Methods: Behavioral subscales were defined as follows: Mood (depression/dysphoria, anxiety, irritability/lability, night-time behavior disturbances, appetite/eating change), Psychosis (delusions, hallucinations, agitation/aggression), Frontal (euphoria/elation, disinhibition), or Other (apathy, aberrant motor behavior). A positive response for each subscale was defined as no net change or net improvement on the NPI items constituting the subscale. *P* values were based upon a CMH test controlling for study center.

Results: Results (OC) indicate that memantine had a significant effect over placebo upon symptoms in the Mood subscale at both weeks 12 (P=.034) and 24 (P=.033), with 65.5% of patients in the memantine group showing a positive response at week 24. Memantine also had a significant effect over placebo (OC) upon symptoms of Psychosis at both weeks 12 (P=.006) and 24 (P<.001), with 80.7% of patients in the memantine group showing a positive response in this domain at week 24. The response difference (OC) between memantine and placebo patients at week 24 was 12.2% and 18.9% for Mood and Psychosis subscales, respectively. LOCF analysis yielded comparable results. Effects of memantine on Frontal symptoms were not significant, while the effects on Other symptoms were significant at week 24 using LOCF analysis (P=.037), but not OC analysis (P=.058).

Conclusions: Taken together, these results suggest that memantine provides specific behavioral benefits for mood and psychosis-related symptoms associated with AD.

References:

1. Frisoni GB, Rozzini L, Gozzetti A, et al. Behavioral syndromes in Alzheimer's disease: description and correlates. Dement Geriatr Cogn Disord. Mar-Apr 1999;10(2):130-138.
2. Tariot PN, Farlow MR, Grossberg GT, et al. Memantine treatment in patients with moderate to severe Alzheimer disease already receiving donepezil: a randomized controlled trial. JAMA. 2004;291(3):317-324.

NR908 Thursday, May 25, 12:00 PM - 2:00 PM

Post Concussion Symptom Check List and Automated Neuropsychological Assessment Metrics in Assessment of Traumatic Brain Injury in Blast Victims

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Educational Objectives:

At the conclusion of the session participants should be able to conduct neuropsychiatric screenings of blast victims to recognize TBI apart from psychiatric conditions, refer for assessment of cognitive impairment, and recommend fitness for return to duty.

Summary:

Introduction: Blast injury occurs commonly in Iraq/Afghanistan war, with 59 % of blast patients seen 1/03 - 4/05 at Walter Reed Army Medical Center having sustained a TBI (1). The majority of patients have closed TBI. Military, federal and civilian contractors and Iraqi civilians are also exposed to blast injuries. Acute stress reactions can cloud diagnosis of TBI. Clinical instruments to assess TBI in blast victims may assist the clinical evaluation during individual and mass casualties.

Method: A self-report symptom survey, the PCSC and a computerized cognitive battery, ANAM (2) were used to evaluate 27 victims on-site after a 7-story Baghdad hotel bombing by a truck carrying 2000+ pounds of explosives, blowing out all the windows and doors.

Results:

17/27 (62.9%) people had amnesia for seconds to minutes surrounding the event.

10/17 (58.8%) had PCSC score >50.

5/17 (29.4%) with the highest PCSC scores tested with ANAM within 48 hours showed significant cognitive deficits (2 SD below norm). 4/5 retested by three weeks had recovered fully.

Conclusion:

Combined use of PCSC and ANAM is a field expedient tool to recognize TBI in monitoring blast victims' recovery, to aide return to duty decisions and avoid possible exposure to re-injury before full recovery.

References:

1. Okie S: Traumatic Brain Injury in the War Zone. N Engl J of Med 2005; 352 (20): 2043-7.
2. Bleiberg J, Kane RL, Reeves DL, Garmoe WS, Halpern E: Factor analysis of computerized and traditional tests used in mild brain injury research. Clin Neuropsychol 2000; 14 (3): 287-94.

NR909 Thursday, May 25, 12:00 PM - 2:00 PM

A Prospective Study of Cognitive Performance in Amnestic MCI Using Comprehensive Computerized Assessment

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to appreciate the ability of a set of computerized cognitive tests to identify different cognitive profiles in MCI individuals declining at 1-year follow-up as compared with those not declining.

Summary:

Objective: To compare the cognitive profile of mild cognitive impairment (MCI) individuals declining after 1-year with those not declining in an ongoing two-site multiethnic cohort study.

Method: Participants were 44 MCIs (Petersen's criteria for amnestic MCI; age: 72.4±10.1; education: 13.8±4.1) and 21 controls (age: 72.7±11.2; education: 15.2±3.1) in a prospective study who completed the Mindstreams® Global Assessment Battery (NeuroTrax Corp., NY) at baseline and 1-year. MCIs were defined as "decliners" or "non-decliners" depending upon 1-year 'MCI Score' classification. Between-groups analysis was by Mann-Whitney *U*

test. Dependent measures were age- and education-normalized Memory, Executive Function, Visual Spatial, and Attention summary scores, a Global Cognitive Score summarizing battery performance, and Lawton iADL category scores.

Results: MCI decliners performed worse than controls at 1-year in executive function (p=0.02), visual spatial (p=0.04), and global performance (p=0.009). In contrast, change in non-decliners was not different from controls for any measure (p's>0.11). MCI decliners exhibited greater change than MCI non-decliners in executive function (p<0.001), attention (p=0.04) and battery performance (p=0.007); decliners also performed worse in ability to use the telephone (p=0.03). MCI decliners performed more poorly at baseline in executive function (p=0.005) and attention (p=0.04); decliners were also more functionally dependent in telephone use (p=0.003), shopping (p=0.02), and food preparation (p=0.02).

Conclusions: Computerized cognitive assessment can assist clinicians in identifying MCI patients likely to convert to dementia. These preliminary findings suggest that executive function at baseline is an important predictor of subsequent cognitive decline in amnestic MCI.

References:

1. Dwolatzky T, Whitehead V, Doniger GM, Simon ES, Schweiger A, Jaffe D, Chertkow H: Validity of a novel computerized cognitive battery for mild cognitive impairment. BMC Geriatr 2003; 3:4.
2. Doniger GM, Zucker DM, Schweiger A, Dwolatzky T, Simon ES: Towards practical cognitive assessment for detection of early dementia: a 30-minute computerized battery discriminates as well as longer testing. Curr Alzheimer Res 2005; 2:117-124.

NR910 Thursday, May 25, 12:00 PM - 2:00 PM

Computerized Cognitive Tests for Traumatic Brain Injury Correlate With Standard Tests of Malingering Detection

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to: a) evaluate the discriminant validity of a set of computerized cognitive tests in measuring cognitive impairment associated with traumatic brain injury (TBI), and b) appreciate the relationship between performance in particular cognitive domains and malingering.

Summary:

Objective: To assess the validity of Mindstreams computerized cognitive tests in identifying cognitive sequelae of traumatic brain injury (TBI) and to define the cognitive correlates of standard tests of malingering.

Methods: 23 patients with mild TBI (age: 34.2±14.3; years of education: 12.3±2.4) and 23 age- and education-matched controls completed the Mindstreams® Global Assessment Battery (NeuroTrax Corp., NY). Nine TBI patients were suspected of malingering on the basis of both the Rey 15-Item and Test of Malingering in Memory (TOMM), standard tests for malingering detection that are simple memory tests described to the patient as difficult. Discriminant validity was assessed by between-groups t-test and area under the curve (AUC) from receiver operating characteristic (ROC) analysis. Pearson correlations were computed in patients between Rey-15 and TOMM and Mindstreams measures. Primary dependent measures were Memory, Executive Function, Visual Spatial, and Attention summary (index) scores and a Global Cognitive Score (GCS) summarizing battery performance.

Results: The Mindstreams Memory index score was near-perfect (AUC=0.99) at discriminating TBI from cognitively healthy (t_{38}=11.43, p<0.001), followed by Executive Function (AUC=0.94; t_{39}=8.00, p<0.001), Attention (AUC=0.94; t_{40}=7.41, p<0.001), and Visual Spatial (AUC=0.79; t_{33}=3.24, p=0.003). Discrimination was near-perfect for the global measure summarizing battery performance (GCS: AUC=0.99; t_{39}=10.10, p<0.001). Both Rey 15-item (r=0.66, p=0.003) and TOMM (r=0.52, p=0.02) correlated with Executive Function but neither correlated with Memory (p's>0.032).

Conclusions: Mindstreams tests exhibit excellent discriminant validity for detecting cognitive sequelae of mild TBI and show correspondence between standard tests of malingering and executive function, suggesting that malingering may be best detected on computerized tests of executive function.

References:

1. Dwolatzky T, Whitehead V, Doniger GM, Simon ES, Schweiger A, Jaffe D, Chertkow H: Validity of a novel computerized cognitive battery for mild cognitive impairment. BMC Geriatr 2003; 3:4.
2. Doniger GM, Dwolatzky T, Zucker DM, Chertkow H, Crystal H, Schweiger A, Simon ES: Computerized cognitive testing battery identifies MCI and mild dementia even in the presence of depressive symptoms. Am J Alzheimers Dis Other Demen 2006.

NR911 Thursday, May 25, 12:00 PM - 2:00 PM

Measuring Functional Ability in Schizophrenia

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to summarize the psychometric characteristics of a newly developed and validated objective functionaing instrument in schizophrenia, and to use it in future research.

Summary:

Objective: Research in schizophrenia has demonstrated a link between cognitive impairment and functioning. Hence a measure quantifying objective functioning is needed to fulfill regulatory requirements for medications targeting cognitive impairment. The Schizophrenia Objective Functioning Instrument (SOFI) was created to meet this need. Expert consensus led to identification of 4 domains: living situation, instrumental activities of daily living, productive activities and social functioning. Domain items were evaluated by experts followed by focus groups of patients and informants to formalize objective measures. Interviewers complete 4 global domain scores (1 (worst)-100) following a semi-structured discussion with patient or informant and close-ended item ratings on level of independence and assistance needed. The psychometric characteristics of the SOFI are presented in this study.

Methods: 104 stable schizophrenia/schizoaffective outpatients and informants completed the SOFI at 9 US CATIE (Clinical Antipsychotic Trials in Intervention Effectiveness) clinical centers. Source concordance and reliability were determined. Validity was established against the PANSS, Brief Assessment of Cognition in Schizophrenia (BACS) scales and living situation.

Results: The majority of patients (66.3%) were male (mean age 42.3). 80% were diagnosed with schizophrenia. Only 20% reported having a psychiatric hospitalization within the past year. Almost half (46.2%) of informants characterized themselves as paid informants. Informant and patient agreement was good ranging from 0.65 (Social Function) to 0.80 (Productive Activities); test-

retest reliability was excellent (ICCs from 0.66-0.94). SOFI scores differentiated between patients with high and low scores on both PANSS and BACS. Patients in unrestricted living situations demonstrated better functioning than those in restricted living.

Conclusion: High reliability and validity were observed on patient/informant reports of patient's ability to function in major domains. Patients with fewer symptoms and/or less cognitive impairment demonstrate higher SOFI scores providing initial evidence that the SOFI is responsive to change over time.

References:

1. Green MF, Kern RS, Braff DL, Mintz J: Neurocognitive deficits and functional outcome in schizophrenia: are we measuring the "right stuff"? Schizophr Bull 2000;26(1):119-136.
2. Purdon SE, Jones BD, Stip E, et al.: Neuropsychological change in early phase schizophrenia during 12 months of treatment with olanzapine, risperidone, or haloperidol. Arch Gen Psychiatry 2000;57(3):249-258.

NR912 Thursday, May 25, 12:00 PM - 2:00 PM

The Relationship Between Head Injuries, Homicide, and Violence

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Educational Objectives:

Educational Objectives:

At the conclusion of this presentation participants will be aware of the strong relationship between prior head injury and subsequent participation in violence and homicide.

Summary:

Although there has been much research on the neurobehavioural sequelae of head injury, few studies have examined the incidence of closed head injuries in violence and homicide. Eastern Kentucky has an extremely high incidence of head injuries compared to the general population of the United States, which averages 5.8% versus 40% of our in patient population.

Five hundred consecutive admissions to the Appalachian Regional Healthcare (ARH) Psychiatric Center in Hazard, Kentucky were diagnosed by the attending psychiatrists using DSM-IV criteria. All patients were administered a standardized questionnaire by a social worker documenting head injury, family history of alcoholism and drug abuse and patient history of violence and homicide. The relationship of head injuries and violence and homicide was analyzed using Chi square analysis with continuity correction. A probability level of .05 was considered to be significant.

Of the patients in the study, 40% (n = 194) had suffered a closed head injury at some time in their life. Those who had suffered a closed head injury were significantly more likely to have a parent who abused drugs and/or alcohol (p = .0001), to be involved in violence (p = .0001) and to have perpetrated a homicide (p = .0013). They were also significantly more likely to have witnessed violence (p = .0001), to have been a victim of violence (p = .0001), to have witnessed a homicide (p = .0049) and to have suffered emotional trauma (p = .0001). There were no significant differences in the percentage of males and females who had suffered head injuries.

Long term follow up of 500 cases of which 194 had suffered a closed head injury revealed a strong association between prior head injury and later involvement in violence and homicide.

References:

1. Silver, JM., Kramer, R., Greenwald,S., Weissman, M. (2001). The association between head injuries and psychiatric disorders: findings from the New Haven NIMH Epidemiologic Catchment Area Study. Brain Injury, 15(11), pp. 935-945.
2. Ruff, M.R., Crouch, J.A., Troster, A.I. et al. (1994). Selected cases of poor outcome following a minor brain trauma: Comparing neuropsychological and positron-emission tomography assesssment. Brain Inj. 8(4), 297.

NR913 Thursday, May 25, 12:00 PM - 2:00 PM

The Impact of Anxiety, Depression, and Cognitive Impairment on Functioning in the Physically Ill Elderly in Egypt

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Educational Objectives:

At the conclusion of this presentation, the participants should be able to recognize geriatric depression, anxiety state/trait and cognitive dysfunction and their relation to various medical problems as well as their impact on the different forms of functioning. Regardless of its cause, depression requires careful evaluation by the clinician, for it must be disaggregated from other disorders, both physical and psychiatric, so that the most appropriate therapy can be prescribed. Effective treatment and management are available for depression, and timely intervention can reduce the incidence if undesirable consequences in depression such as lowered quality of life, isolation, high mortality rate, diminished functional capacity, added medical morbidity, and suicide.

Summary:

Introduction: In the elderly, depression as well as anxiety are often underdiagnosed in medical settings or simply dismissed as inevitable consequences of aging or unavoidable complication of other illnesses or treatments. So, this study was set out to study the common psychological problems in the physically ill elderly. Depression, anxiety state/trait and cognitive dysfunction and their relation to various medical problems as well as their impact on the different forms of functioning. *Methods:* 100 elderly patients recruited from the inpatient as well as the outpatient clinic in the geriatric department were assessed using Instrumental Activities of Daily Living (IADL), Activities of Daily Living (ADL), health promotion questionnaire, Mini Mental State (MMS), Geriatric Depression Scale (GDS, *30 items)*, State-Trait Anxiety Inventory (STAI), as well as assessment for the different medical conditions. *Results:* Only 26% had *mild* cognitive impairment according to MMS, 64% were depressed according to GDS & 72% were suffering from anxiety as assessed by SAST & 35% had anxiety trait by the same scale. Moreover, 47% were dependant as regards IADL and 26% as regards ADL. Neither depression nor anxiety trait were associated with any sociodemographic or clinical variables ($P>0.05$). However, anxiety state was highly significantly associated ($P<0.01$) with perceived decline in functioning. *Conclusion:* Regardless of their cause, depression as well as anxiety should be disentangled from any other disorder, particularly from physical disorders, so that the most appropriate treatment can be prescribed as timely intervention can reduce the incidence of undesirable consequences including suicide.

References:

1. Blazer DG: Psychiatric Disorders. In The Merck Manual of Geriatrics, edited by Beers MH and Berkow R, New Jersy, Merck & Co., 2000, pp 307-341.
2. Omar AN, Haroun A, Nagy NE: Prevalence of depressive symptoms in physically-ill elderly inpatients. Current Psychiatry 1998; 5 (2):145-155.

NR914 Thursday, May 25, 12:00 PM - 2:00 PM

The Effects of Rivastigmine, Donepezil, and Galantamine on Cholinesterase Activity in CSF of Alzheimer's Disease Patients

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Educational Objectives:

At the conclusion of this session participants will know that there are different effects on cholinesterase activity in the CSF of patients treated with different ChEIs.

Summary:

Objective: To evaluate and compare in patients with Alzheimer's disease (AD) the effects of rivastigmine, donepezil, and galantamine on cholinesterase activity in CSF in an open-label, randomized study.

Background: Levels of acetylcholine (ACh) fall sharply in the brains of patients with AD and cognitive deficits correlate with this loss. Current treatment for AD is based on rectifying the cholinergic deficit by inhibiting cholinesterase enzymes. While both acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE) are involved in regulating cholinergic neurotransmission, BuChE activity has been found to markedly increase as AD progresses.

Methods: Analysis of 13-week data from an open-label, multicenter study in mild-to-moderate AD patients randomized to treatment with rivastigmine, donepezil or galantamine. Measurement of BuChE and AChE in the CSF was done by colorimetric determination. Treatment effects were assessed using the Clinical Global Impression of Change (CGIC).

Results: Sixty-three patients with a mean age of 74.9 years and a mean duration of dementia of 3.0 years are included; 69.8% (n=44) were female. Approximately 77% of patients reported at least one AE (overall; 86.4% rivastigmine, 65% donepezil, 81% galantamine). Preliminary analyses indicated that at Week 13, BuChE activity was decreased in the rivastigmine group and increased or stable in the donepezil and galantamine groups. Acetylcholinesterase activity was decreased in the rivastigmine group and increased in the other two treatment groups. When compared to rivastigmine, between-group differences of changes in both BuChE and AChE activity were statistically significantly different. The mean rating of change on the CGIC for rivastigmine, donepezil, and galantamine was 4.0, 4.2 and 4.1, respectively (ITT population/LOCF analysis).

Conclusions: These are preliminary findings; however, there appear to be differential effects on cholinesterase activity in CSF with different ChEIs. The clinical significance of these findings is under further investigation.

References:

1. Giacobini E, Spiegel R, Enz A, et al (2002) Inhibition of acetyl- and butyryl-cholinesterase in the cerebrospinal fluid of patients with Alzheimer's disease by rivastigmine: correlation with cognitive benefit. J Neural Transm; 109(7-8):1053-65.
2. Greig N, Utsuki T, Qian-sheng Y, et al (2001) A new therapeutic target in Alzheimer's disease treatment: attention to butyrylcholinesterase. Cur Med Res Opin; 159-165.

NR915 Thursday, May 25, 12:00 PM - 2:00 PM

The Safety and Efficacy of Rivastigmine Plus Memantine Versus Rivastigmine Monotherapy in Mild to Moderate Alzheimer's Disease

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Educational Objectives:

The goals of this study are to examine the safety and efficacy of combined Rivastigmine (R) (a dual inhibitor of butyrylcholinesterase and acetylcholinesterase) and M therapy versus R monotherapy in patients with mild to moderate AD, and to specifically examine whether the R and M group has a reduction in GI side-effects.

Summary:

Introduction: Memantine (M) is a noncompetitive *N*-methyl-D-aspartate receptor antagonist. Controlled studies have demonstrated the efficacy of M in the treatment of patients with Alzheimer's disease (AD),[1] and these studies have also suggested the M may reduce the incidence of gastrointestinal (GI) side-effects from cholinesterase inhibitors through its ability to inhibit the 5HT3 receptor.[2]

Methods: a six month prospective pilot, single blind clinical trial of 82 patients with mild to moderate AD who received either R plus M or R alone. The dosages of R and M were administered according to a predetermined protocol. A total of 70 (85%) patients completed the study.

Results: Patients receiving R plus M had a significantly higher increase in their MMSE scores at 6 months compared with the patients who received R alone. (1.88 versus .68) ($p < .05$)

The Clinician's Interview Base Impression of change (CIBIC Plus) scores were significantly improved in the R plus M group compared with patients treated with R alone. (Improved 23/35 versus 12/35) ($p< .02$)

32/35 (92%) patients receiving R plus M were able to tolerate R doses > 6 mg versus 20/35 (58%) receiving R alone. ($p < .02$)

Conclusion: In patients with mild to moderate AD the combination of R and M resulted in significantly better outcomes than R alone in measures of cognition and global outcomes. In addition, patients who received R plus M were able to tolerate higher doses of R due to a reduction in GI side-effects. The question of whether the potential clinical benefits of combined R plus M therapy over R monotherapy observed in this study are related to the combined different mechanisms of action for R and M or due to an increased percentage of patients tolerating higher doses of R will be discussed.

References:

1. Journal Article: Tariot PN, et al., Memantine Treatment in Patients with Moderate to Severe Alzheimer's Disease Already Receiving Donepezil A Randomized Controlled Trial. Jama, January 21, 2004; 291(3):317-314.
2. Bullentin: Drug Therapy Bullentin. 5HT3-receptor antagonists as antiemetics in cancers. Drug Ther Bull., 2005: 43(8):57-62.

NR916 Thursday, May 25, 12:00 PM - 2:00 PM

The Impact of Depression on the Accuracy of Subjective Memory Complaints in Geriatric Patients

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Educational Objectives:

At the conclusion of this presentation the participant should be able to :

i) Establish that there are two factors which may affect the accuracy of subjective memory complaints in older persons_neurocognitive impairment and depressive symptoms.

ii) Establish that it is important to distinguish depressive symptoms associated with objective cognitive impairment from depressive symptoms associated with normal cognitive functioning as they may arise from different disease mechanisms, have differ-

ent treatment responses and may influence the accuracy of reporting of memory symptoms in different ways.

Summary:

Objective: The aim of the study is to evaluate the relationship between memory complaints and actual performance on neuropsychological dimensions and to determine if depressive symptoms play a role.

Methods: Seventy-three patients were recruited from a Memory Disorders Clinic (age > 55 years). Subjects who met established inclusion and exclusion criteria were administered a variety of neurocognitive tests. Measures included level of subjective memory complaints, depressive symptoms, verbal memory, working memory, and attention. Four patient subgroups were identified based on combinations of subjective memory complaints (Patient's Assessment of Own Functioning) and objective memory performance (California Verbal Learning Test-II). "Accurate -normal" (n=25; normal memory and low memory complaints), "accurate-impaired" (n=12; impaired memory and high memory complaints), "over-reporters" (n=20; normal memory and high memory complaints) and "minimizers" or under-reporters (n=16; impaired memory and low memory complaints).

Results: The groups did not differ significantly in terms of age or education. Patients with Alzheimer's disease were over-represented among minimizers (p<.01). Accurate-impaired and over-reporter subgroups had significantly more mood complaints than the accurate-normal and minimizer subgroups. In terms of neuropsychological functioning, the accurate-normal and over-reporter groups performed significantly better on measures of verbal memory and working memory, compared to the other two groups (accurate-impaired and minimizers). The minimizer subgroup was found to perform significantly worse on measures of attention and verbal recognition.

Conclusion: Memory complaints appear to be related to increases in mood disturbance (depression), and also to cognitive functioning (i.e, cerebral impairments). Being able to reliably differentiate those who have cognitive (brain) impairments with depression and those who are depressed without a cognitive impairment is important because the treatments for each are different.

References:

1. Jungwirth S, Fischer P, Weissgram S, Kirchmeyr W, Bauer P, Tragl KH. Subjective memory complaints and objective memory impairment in the Vienna-Transdanube aging community. J Am Geriatr Soc. 2004 Feb;52(2):263-8.
2. O'Connor DW, Pollitt PA, Roth M, Brook PB, Reiss BB. Memory complaints and impairment in normal, depressed, and demented elderly persons identified in a community survey. Arch Gen Psychiatry. 1990 Mar; 47(3):224-7.

NR917 Thursday, May 25, 12:00 PM - 2:00 PM

Delirium Symptoms in Patients From the Intensive Care Unit

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to know the most common delirium symptoms at the intensive care unit

Summary:

Introduction: The purpose of this study was to determine delirium symptoms in patients from the intensive care unit. Symptoms reported elsewhere had not been from this population. We found several symptoms ranging from disorientation to perceptual disturbances.

Objective: Determine delirium symptoms in patients from the intensive care unit

Methods:

Design: Prospective

Setting: a tertiaty care referral center

Intervention:We used the structured instrument for the diagnosis of delirium and its measurement for the intensive care unit. One hundred and forty (intubated/non intubated and sedated/non sedated) patients were evaluated, seventy of them developed delirium. The instrument evaluates attention, orientation (person, circumstance, month, place), judgment, recent memory, retention memory, concentration, auditive hallucinations, visual hallucinations, tactile hallucinations and delusions.

Main outcome measure:delirium

Results:Frequencies are described : Attentional deficits 100%, severe attention impairment 12.5%, disorientation in month, person and circumstance 6.3% each, disorientation in year 25%, judgment 20.3%,concentration 17.2%, retention memory 37.5%, recent memory 26.6%, auditive hallucinations 32.8%, visual hallucination 35.9%, tactile hallucinations 29.7%, delusions 21.9%

Conclusions:

As it is expected 100% had an attention disturbance but only 12% had a severe attention impairment, it is likely that memory disturbances might be related to these attention and concentration disturbances.

Disturbance in orientation in year was the more frequent type of orientation impairment.

Visual hallucinations was the more frequent among the perceptual disturbances.

References:

1. Trzepacz et al. Neuropsychiatric aspects of delirium, American Psychiatric Press Textbook of Neuropsychiatry, 4th edition, Washington D.C., APPI 2001.
2. Trzepacz P.T. Sem Clin Neuropsychiatry, 2000, 132-148.

NR918 Thursday, May 25, 12:00 PM - 2:00 PM

The Sociodemographic and Phenomenological Features of Brazilian Patients With BDD

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that, despite the increasing importance of physical attractiveness in the modern Brazilian society, it seems that the phenomenological features of Brazilian patients with body dysmorphic disorder are undistinguishable from those reported in developed countries.

Summary:

Objective: The main characteristic of BDD is a preoccupation with an imagined defect in the appearance of a normally appearing person or an excessive preoccupation with appearance in a person with a small physical defect. In this study, our objective was to describe the socio-demographic and phenomenological characteristics of a Brazilian sample of 20 patients with BDD.

Method: Chart-review.

Results: Our sample was characterized by a predominance of female (n=11; 55%), single or divorced (n=18; 90%) and economi-

cally unproductive patients (n=17; 85%). A current preoccupation with an average of more than 2 imagined defects was found, more commonly located on the skin (n=6; 37.5%), overall body build (n=6; 37.5%) and hair (n=5; 31.2%). Most patients exhibit a chronic condition (n=13; 65%) and had the same concerns during the course of the disorder (n=13; 65%). All patients exhibited compulsive behaviors, including excessive mirror checking (n=14; 70%), camouflaging (n=13; 65%), reassurance seeking (n=9; 45%) and excessive use of cosmetics (n=7; 35%). Two patients reported "do-it-yourself" surgeries. Seven patients displayed suicidal ideation (35%). Six patients (30%) had no insight over their dysmorphic beliefs. Fifteen patients (95%) exhibited psychiatric comorbidities, including OCD [n=14, 70%] and MDD (n=11; 55%). The majority of patients were treated naturalistically with 5HT reuptake inhibitors (n=15; 75%), either solo or together with antipsychotics (n=9; 45%). Nevertheless, only 3 (15%) responded to treatment (CGI â‰¤ 2).

Conclusions: BDD is a severe psychiatric disorder that is frequently associated with other psychiatric conditions and responds poorly to treatment in the naturalistic setting.

References:

1. Phillips KA, McElroy SL, Keck PE Jr, Pope HG Jr, Hudson JI: Body dysmorphic disorder: 30 cases of imagined ugliness. Am J Psychiatry 1993; 150: 302-308.
2. Veale D, Boocock A, Gournay K, Dryden W, Shah F, Willson R, Walburn J: Body dysmorphic disorder. A survey of fifty cases. Br J Psychiatry 1996, 169: 196-201.

NR919 Thursday, May 25, 12:00 PM - 2:00 PM

Pathological Gambling and Dopamine Agonist Therapy in Parkinsonism: A Case Report

Rafael Ferreira-Garcia, M.D. *Rio de Janeiro*, Bruno P. Nazar, M.D., LÃdia Ordacgi, M.D., Gabriel R. de Freitas, M.D., Ana LÃcia Z. Rosso, M.D., Mauro V. Mendlowicz, M.D., Leonardo F. Fontenelle, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that pathological gambling may be a side-effect of the dopamine agonist therapy in parkinsonism.

Summary:

Background: Pathological gambling was recently recognized as a rare side effect of the treatment of Parkinson's disease with dopaminergic agonists. This phenomenon may be more common during the treatment with pramipexole, a D3 dopaminergic receptor selective agent. Since only a handful of such cases have been reported so far, there is still no consensus regarding the best treatment options for these patients. In this study, our objective was to present the case and the management of a patient with a drug-induced pathological gambling.

Method: Case report.

Results: Our patient, who had Juvenile Parkinson's disease, developed an incontrollable urge to gamble soon after the beginning of treatment with pergolide, a dopaminergic agonist. This behavior remitted after the drug discontinuation, along with the worsening of the motor signs and symptoms. Moreover, the introduction of another dopaminergic agonist, pramipexole, resulted in the recurrence of the pathological gambling. The management of this side effect involved the reduction of this latter drug.

Conclusions: Our case suggests that patients with parkinsonism may develop pathological gambling as a side-effect of more than one dopaminergic agonist. It also suggests that dopaminergic hyperactivity plays an important role in pathological gambling and in other impulse control disorders.

References:

1. Dodd ML, Klos KJ, Bower JH, Geda YE, Josephs KA, Ahlskog JE. Pathological gambling caused by drugs used to treat Parkinson disease. Arch Neurol. 2005; 62:1377-81.
2. Avanzi M, Uber E, Bonfa F. Pathological gambling in two patients on dopamine replacement therapy for Parkinson's disease. Neurol Sci. 2004; 25: 98-101.

NR920 Thursday, May 25, 12:00 PM - 2:00 PM

A Three-Year Follow-up of Major Depression, Dysthymia, Minor Depression, and Subsyndromal Depression. Results From a Population-Based Study.

Yvonne Forsell *Public Health Science, Karolinska Institutet, Stockholm, Sweden, Social Medicine, Karolinska hospital, Norrbacka, Stockholm, S-17173, Sweden*

Educational Objectives:

The study gives information on the prognosis and stability of different categories of depression.

Summary:

Objective This study examined the three-year outcome of Major Depression (MD), Minor Depression (MinD), Subsyndromal Symptomatic Depression (SSD) and Dysthymia in a population based sample. The aims were to compare the stability and to analyze the risk of fulfilling the criteria for MD at the follow-up.

Method An extensive questionnaire was sent out to persons aged 20-64 years registered in the Stockholm county. Depression was assessed using the Major Depression Inventory. After three years the procedure was repeated. 8 622 persons participated in both waves. Diagnoses of MD, Dysthymia, MinD, SSD were made. Various characteristics were analyzed as potential prognostic factors.

Results Of those affected by any of the depressive disorders at wave one (n=1 652) 50% were also affected at wave two. Highest three-year stability was found in MD and lowest in Dysthymia. The risk of fulfilling the criteria for MD at wave two was highest for those affected by MD (RR 26.4) at wave one, followed by those affected by Dysthymia (RR 8.0). Those affected by MinD or SSD had similar rates (RR 4.9 and 4.4). Hazardous use of alcohol, somatic disorders, anxiety symptoms and negative life events were found to be associated with depression at wave two.

Conclusions MD had the highest stability as well as the highest risk of MD at the three-year follow up. MinD and SSD had similar risks.

References:

1. Judd LJ, Akiskal HS, Maser JD, Zeller PJ, Endicott J, Coryell W, Paulus MP, Kunovac JL, Andrew CL, Mueller TI, Rice JA, Keller MB: A prospective 12-year study of subsyndromal and syndromal depressive symptoms in unipolar major depressive disorders.
2. Judd LL, Akiskal HS, Paulus MP: The role and clinical significance of subsyndromal depressive symptoms (SSD) in unipolar major depressive disorders. J Affect Disord 1997;45(1-2):5-17.

NR921 Thursday, May 25, 12:00 PM - 2:00 PM

Behaviorally-Defined Executive Function Deficits Associated With Academic, Interpersonal, and Occupational Deficits in Adults With ADHD: A Controlled Study

Ronna Fried, Ed.D. *Boston, MA*, Carter Petty, Michael C. Monuteaux, Eric Mick, Sc.D., Joseph Biederman

Educational Objectives:

At the conclusion fo thie presentation, the participant should be able to understand that presence of behaviorally-defined EFDs in ADHD subjects was associated with significant functional morbidity beyond that conferred by the diagnosis of ADHD alone.

Summary:

One of the suspected sources of the morbidity and disability associated with ADHD has been deficits in a group of neuropsychological functions known as executive functions (EF). Considering the critical importance of EF for normal functioning (Barkley, 2001), it is reasonable to assume that EFDs are very likely to be associated with functional impairments. The main aim of this study was to evaluate the impact of behaviorally-defined EFDs on the functional outcomes of adults with and without ADHD. To this end, we used the Barkley CBS to define behavioral concomitants of EFDs in a large sample of well- characterized adults with and without ADHD. We hypothesized that behaviorally-defined EFDs would be associated with deficits in educational, occupational and interpersonal functioning.

Subjects, aged 18 thru 55 with DSM-IV ADHD, were eligible for this study. Barkley's Current Behavior Scale (CBS), a 99-item self-report questionnaire, was used to assess behavioral concomitants of executive function deficits. We defined three groups: adults without ADHD (Control, N=140), adults with ADHD without EFDs (ADHD, N=101), and adults with ADHD with EFDs (ADHD+EFD,N=99).

The Control group had a mean total CBS score of 31.7 (SD= 22.5), the ADHD group had a mean CBS score of 99.9 (SD=30.2), and the ADHD+EFD group had a mean score of 184.8 (SD=31.0). The ADHD+EFD group had significantly poorer global functioning, and was significantly more impaired on overall social adjustment, work role, social and leisure, extended family, primary relationship, and family unit compared to the ADHD group.

The presence of behaviorally-defined EFDs in ADHD subjects was associated with significant functional morbidity beyond that conferred by the diagnosis of ADHD alone. More efforts are needed to help address EFDs in adults with ADHD.

References:

1. Barkley, R. A. (2001). The executive functions and self-regulation: an evolutionary neuropsychological perspective. Neuropsychology Review, 11, 1-29.
2. Biederman, J., Monuteaux, M., Seidman, L., Doyle, A. E., Mick, E., Wilens, T., et al. (2004). Impact of Executive Function Deficits and ADHD on Academic Outcomes in Children. Journal of Consulting and Clinical Psychology, 72, 757-766.

NR922 Thursday, May 25, 12:00 PM - 2:00 PM

Safety and Efficacy of Lamotrigine (Lamictal®) for Adult Bipolar Disorder Patients Greater Than 55 Years Old

Lawrence D. Ginsberg, M.D. *Red Oak Psychiatry, 17115 Red Oak Drive, Houston, TX, 77090*

Educational Objectives:

At the conclusion of this presentation, the participant should be able understand patient response and tolerability to lamotrigine treatment.

Summary:

Objective: Lamotrigine (Lamictal®) is effective in the treatment of bipolar disorder in adults.[1] This study assessed the effectiveness and safety of lamotrigine (Lamictal®) in adults greater than 55 years of age.

Method: A chart review of 49 outpatients older than 55 years of age with DSM-IV bipolar disorder and treated with lamotrigine (Lamictal®) was conducted (77% female; 55% bipolar I, 31% bipolar II, and 14% bipolar NOS). Charts of subjects who received lamotrigine (Lamictal®) in a private practice setting between October, 1998 and May, 2004 were reviewed. The final mean lamotrigine (Lamictal®) dose was 109.2 ± 90.1 mg/d. Treatment response was assessed with the Clinical Global Impression-Improvement (CGI-I) scale (1 = very marked improvement; 2 = moderate improvement; 3 = minimal improvement). Relapse was defined as a mood change that occurs 4 weeks after initiation of medication or the return of symptoms from the original episode.[2]

Results: Thirty-two subjects (73%) taking lamotrigine (Lamictal®) had marked, moderate, or minimal improvement (CGI-I score: 1, 22%; 2, 53%; 3, 25%), which reflects slightly lower efficacy than in the overall adult population.[2] Nineteen subjects (39%) relapsed and rates were relatively similar among bipolar disorder subtypes. Rates of the most frequently reported side effects, which were non-serious-rash (20%) and insomnia (6%), were higher than those observed in the overall adult patient population.[2]

Conclusion: Lamotrigine (Lamictal®) appears effective in the treatment of bipolar disorder in adult patients older than 55 years of age, though this subpopulation did not respond as well as the overall adult population.[2] Those older than 55 years of age tolerated lamotrigine (Lamictal®) relatively well. These data are encouraging for the use of lamotrigine (Lamictal®) in patients with bipolar disorder who are older than 55 years of age, thus larger scale studies should be undertaken to further investigate these results.

References:

1. Calabrese JR, Bowden CL, Sachs GS, Ascher JA, Monaghan E, Rudd GD. A double-blind placebo-controlled study of lamotrigine monotherapy in outpatients with bipolar I depression. Lamictal 602 Study Group. J Clin Psychiatry. 1999;60:79-88.
2. Ginsberg LD, Safety and efficacy of lamotrigine for adult bipolar disorder patients. APA Poster Presentation, 2005.

NR923 Thursday, May 25, 12:00 PM - 2:00 PM

Practice Patterns Among Physicians Treating Elderly Insomniacs

Harold W. Goforth, M.D. *Duke University Medical Center, Psychiatry and Behavioral Sciences, DUMC 3309, Durham, NC, 27710*, Mugdha E. Thakur, M.D., David C. Steffens, M.D., Andrew D. Krystal, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the incidence and risks of untreated insomnia in the elderly, including psychiatric and medical co-morbidities. Attendees will be able to discuss available evidence in treating insomnia in elderly individuals, and the results of pharmacological studies of hypnotics in the elderly. Participants will, also, be able to recognize current national prescribing patterns for treating elderly insomnics, and differences in prescribing practices across different specialty types as illustrated by the experience of a large academic medical center, and supported by national prescribing database information. At the conclusion of this presentation, attendees will be able to discuss relevant public health concerns and the need for future studies of insomnia to better guide treatment considerations in this vulnerable and growing population

Summary:

Objective: Insomnia is one of the most common problems in the elderly, and has substantial economic and public health consequences including increased falls risk, medical and psychiatric comorbidities, and risk of nursing home placement. However, there is a paucity of systematic research on the pharmacological treatment of insomnia in the elderly, which has been noted repeat-

edly by the National Institutes of Health in multiple Consensus Statements. This lack of available evidence may potentially contribute to a lack of uniformity in treating insomnia, as opposed to other, better-characterized disorders; however, data comparing treatments across specialty types are virtually absent. This study assesses prescribing patterns of psychiatrists as compared to inpatient physicians of all specialties at a large, academic medical center in the treatment of insomnia in patients greater than 60 years of age. Data was obtained by examination of both electronic medical records as well as pharmacy databases. **Results**: Striking differences in prescribing practices were identified across the two groups of physicians. Zaleplon (Sonata®) was the most commonly prescribed hypnotic among all inpatient physicians (82%), followed by temazepam (Restoril®) (9%), zolpidem (Ambien®) (5%), and trazodone (Desyrel®) (4%). However, trazodone (Desyrel®) was the most commonly prescribed hypnotic for the elderly among psychiatrists (40%) followed by zolpidem (Ambien®) (34%), zaleplon (Sonata®) (17%), and temazepam (Restoril®) (9%). **Conclusions**: Hypnotic prescribing patterns of psychiatrists do not appear to be well supported by currently available evidence. Zaleplon (Sonata®) use in the elderly is supported by two large, placebo-controlled trials supporting both its subjective and objective efficacy, whereas there is a paucity of data concerning trazodone's (Desyrel®) efficacy in this population. Additional studies are required to support the use of trazodone as an effective hypnotic agent. In addition, physician education in sleep medicine should be a priority in psychiatric residency training and continuing medical education activities.

References:

1. McCall WV. Diagnosis and management of insomnia in older adults. JAGS. 2005;53:S273-277.
2. James SP, Mendelson WB. The use of trazodone as a hypnotic: a critical review. Journal of Clinical Psychiatry. 20004;B65(6):752-755.

NR924 Thursday, May 25, 12:00 PM - 2:00 PM

Urine Neural Thread Protein (UNTP) in Alzheimer's Disease

Ira Goodman, M.D. *Orlando Regional Healthcare System, 818 Main lane, orlando, FL, 32801*, Greg Golden, M.D., Stephen Flitman, M.D., Kevin Xie, M.D., Alireza Minagar, M.D., Ralph Richter, M.D., Paul Averback, M.D.

Educational Objectives:

Original Research Abstract: A prospective study was carried out to demonstrate the utility of UNTP measurement in the diagnosis of Alzheimer's disease. UNTP measurement provides an improvement of 23% in positive predictive value, and an improvement of 78% in negative predictive value, compared to prior probability based on prevalence. This prospective study confirms earlier retrospective studies of UNTP, and demonstrates its usefulness in the routine evaluation of cases of suspected AD.

Summary:

A prospective study was carried out to demonstrate the utility of UNTP measurement in the diagnosis of Alzheimer's disease. NTP is a 41 kD protein present in neurons which is selectively upregulated in Alzheimer's disease (AD) brain and which is associated with the pathology of the disease. Over-expression of NTP in transfected neuronal cells promotes neuritic sprouting, apoptosis and cell death. Using a new competitive ELISA UNTP assay kit, levels have been measured in samples from cases of AD as well as age matched normal controls and a variety of neurological disease controls (N=168). Levels of greater than 22 μg/mL are found consistently in cases of probable AD and in less than 10% of controls. UNTP measurement provides an improvement of 23% in positive predictive value, and an improvement of 78% in negative predictive value, compared to prior probability based on prevalence. This prospective study confirms earlier retrospective studies of UNTP, and demonstrates its usefulness in the routine evaluation of cases of suspected AD.

Supported in part by funding from Nymox Corporation

References:

1. de la Monte, S. M., et al. Characterization of the AD7C-NTP cDNA expression in Alzheimer's disease and measurement of a 41-kD protein in cerebrospinal fluid. J. Clin. Invest., 1997; 100: 3093-3104.
2. Kahle, P. J., Jakowec, M., Teipel, S. J. et al. Combined assessment of tau and neuronal thread protein in Alzheimer's disease CSF. Neurology, 2000; 54: 1498-1504.

NR925 Thursday, May 25, 12:00 PM - 2:00 PM

Results of an Open-Label Study Evaluating the Safety and Efficacy of Rivastigmine in Patients Not Responding Adequately to Donepezil: Week 52 Analysis

Ibrahim Gunay *Novartis Pharma Corporation, One Health Plaza, East Hanover, NJ, 07936*, John Strigas, Barbara Koumaras, Michael Chen, Yan Yan LiStarkey, Gary Figiel

Educational Objectives:

At the conclusion to this session, participants will know that long-term treatment with rivastigmine is safe and tolerated and may provide a viable therapeutic option to those patients responding poorly to donepezil treatment.

Summary:

Objectives: The objectives of this 26-week, open-label extension were to further evaluate safety and tolerability of rivastigmine in patients with mild-to-moderate Alzheimer's disease (AD) who were responding poorly to or declining while on treatment with donepezil.

Background: AD is a progressive neurodegenerative disorder characterized by a gradual loss of memory and cognitive function, behavioral disturbances, and impairment in activities-of-daily-living. Previous data have shown that switching patients from one cholinesterase inhibitor to another represents a viable therapeutic option for patients who are not responding adequately to current therapy.

Methods: Analysis of data from a 26-week open-label extension to a 26-week open-label, multicenter study assessing the safety and efficacy of rivastigmine 3 to 12 mg/day in patients with mild to moderate AD not responding adequately to donepezil treatment. Patients entered the extension after completing the 26-week study. Safety and tolerability were assessed by the occurrence of adverse events (AEs) and outcomes information was collected at Week 52.

Results: One-hundred forty patients with a mean age of 78.0 (SD=7.22) years and a mean duration of dementia of 3.3 (SD= 1.80) years are included; 62.3% (n=91) were female. Approximately 60% of patients reported at least one AE. The most common AEs which were newly occurring or worsening during the extension were in the following systems: psychiatric (17.85%); neurological (16.4%); gastrointestinal (15.8%). Seven patients (4.8%) discontinued treatment in the extension due to adverse events. Outcomes data collected at Week 52 indicated that 87.7% of patients were still on treatment with rivastigmine. Approximately 77% of patients/caregivers reported that they were satisfied with treatment and nearly 72% of caregivers reported satisfaction with changes in patient's behavior.

Conclusion: These results suggest that long-term treatment with rivastigmine is safe and tolerated in patients who were previously

declining or responding poorly to donepezil and switched to rivastigmine at study baseline.

References:

1. 1. Auriacombe S, Pere J-J, Loria-Kanza Y, et al. (2002) Efficacy and safety of rivastigmine in patients with Alzheimer's disease who failed to benefit from treatment with donepezil. Cur Med Res Opin, 18(3), 129-138.

2. 2. Shua-Haim J, Smith JM, Amin S. Crossover results from donepezil (Aricept) to rivastigmine (Exelon) in Alzheimer's disease patients: an overall analysis of 3 prospective studies. Poster presented at: American Geriatrics Society Annual Meeting; May.

NR926 Thursday, May 25, 12:00 PM - 2:00 PM

Discrepancies Between *DSM-IV* and *ICD-10* criteria for PTSD

Gökben Feride Hizli *Baskent University, Department of Psychiatry, 10. Sokak No:24/1 Bahcelievler, Ankara, 06000, Turkey*, Nilgün Taskintuna, Sedat Isikli, Leyla Zileli

Educational Objectives:

At the conclusion of this presentation, the participant should be able to demonstrate researches and epidemiological studies will be hampered by the discrepancies between the diagnostic systems. The results of the present study shows that assumption of equivalency between ICD-10 and DSM-IV criteria for PTSD needs further testing.

Summary:

Introduction: Researches and epidemiological studies will be hampered by the discrepancies between the diagnostic systems[1].The aim of this study was to examine whether the participants receiving an ICD-10 diagnosis of Posttraumatic Stress Disorder (PTSD) will also receive a DSM-IV diagnosis of PTSD.

Methods: Data were obtained for 90 participants who survived the Marmara earthquake. The Composite International Diagnostic Interview 2.1 used to assess the PTSD for DSM-IV and ICD-10 Diagnostic Criteria for Research (ICD-10 DCR).

Results: Thirty-two of ninety participants did not get a diagnosis of PTSD on either diagnostic system. 46.7% (n=42) of participants were given a diagnosis of PTSD by both diagnostic systems. Thus there was 82.2% agreement between the two diagnostic systems. The 12 month prevalence of PTSD in this sample is 46.7 % (42 out of 90) when DSM-IV criteria used, 64.4 % (58 out of 90) when ICD-10 DCR used. 68.8 % of discrepancies between two diagnostic systems occurred because participants were negative for DSM-IV criterion C but positive for ICD-10 DCR criterion C.

Conclusion: Some differences exist between the PTSD diagnostic criterion presented in the ICD-10 DCR and DSM-IV[2]. The additional construct of general numbing of responsiveness in DSM-IV criterion C found to be an important cause of discrepancies between DSM-IV and ICD-10 DCR. The results of the present study shows that assumption of equivalency between ICD-10 and DSM-IV criteria for PTSD needs further testing.

References:

1. Andrews G, Slade T: The classification of anxiety disorders in ICD-10 and DSM-IV: A concordance analysis. Psychopathology 2002; 35:100-106.

2. Peters L, Slade T, Andrews G: A comparison of ICD10 and DSM-IV criteria for Posttraumatic Stress Disorder. Journal of Traumatic Stress 1999; 12, 2:335-343.

NR927 Thursday, May 25, 12:00 PM - 2:00 PM

Psychiatric Comorbidity of Internet Addiction in Children and Adolescents

Jee Hyun Ha, M.D. *Yongin Mental Hospital, Department of Psychiatry, Sangha-ri 4, Kusung-eup, Yongin, 449-769, Republic of Korea*, Hee Jung Yoo, M.D., In Hee Cho, M.D., Dongkeun Shin, M.D., Bumsu Chin, M.D.

Educational Objectives:

This is the first study performing structured interview to subject with internet addiction in children and adolescence. According to the findings in this presentation, the participants should be able to understand the underlying causes of so-called 'internet addiction'. The cause of internet addiction differs with age ; most frequent reason for children is ADHD, and depression for adolescent. This presentation can help clinicians to evaluate the problematic internet users.

Summary:

Objectives: This study is aimed to evaluate the clinical comorbidity of internet addiction subjects by structured interview with children and adolescents.

Methods: We selected 12 children (male=9, female=3) and 12 adolescents (male=11, female=1) who were considered to have internet addiction after screening 455 children (age=11.0±0.9) and 836 adolescents (15.8±0.8), according to the Young's internet addiction scale (IAS). We performed K-SADS-PL-K on children and SCID-IV on adolescents to evaluate their current psychiatric diagnosis.

Results: Mean IAS score was 59.41±8.87 in the children's group. 7 were diagnosed with ADHD NOS including subthreshold level. In adolescent group, mean IAS score was 76±12.5. 3 subjects had MDD; 1 had schizophrenia, and one other had OCD. No subject could be diagnosed as 'impulse control disorder NOS'

Conclusion: By structured interview, internet addiction is closely related to ADHD in children and MDD in adolescents. The cause of internet addiction differs with age. Nearly half of the subjects had major psychiatric disorders in both groups. In the case of internet addiction, clinicians must consider the possibility of age specific comorbid psychiatric disorders.

References:

1. Black DW, Belsare G,Schlosser S. Clinical features, psychiatric comorbidity, and health-related quality of life in persons reporting compulsive computer use behavior. J Clin Psychiatry 1999;60:839-44.

2. Shapira NA, Goldsmith TD, Keck PE, Jr., Khosla UM,McElroy SL. Psychiatric features of individuals with problematic internet use. J Affect Disord 2000;57:267-72.

NR928 Thursday, May 25, 12:00 PM - 2:00 PM

A Tale of Three Funding Cultures: How Funding for Primary Care Influences the Provision of Collaborative Care

John M. Haggarty, M.D. *Lakehead Psychiatric Hospital, 580 North Algoma Street, Thunder Bay, ON, P7B 5G4, Canada*, Jennifer Lehto, R.N.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to describe the variation among three major primary care clinics in Thunder Bay, Ontario, Canada currently providing Shared Mental Health Care Services and differences in the clinics' capacity to engage in the full collaborative process. The participant should develop an awareness of strategies to enhance capacity and cooperation when working within these three funding models of Fee-for-Service, Capitation, and Health Service Organization.

Summary:

Shared Mental Health Care services have been provided in Thunder Bay, Ontario, Canada for nearly five years. We will describe how during this time, expansion began from a Fee-for-Service clinic that moved to a Family Health Team as reflective of the changes to primary health care funding. In addition, this presentation will summarize how expansion into Community Health Centres, and large group Fee-for-Service clinics differ in their capacity to engage with the full collaborative process. We will attempt to describe the various means in which the relationship varies between mental health providers and primary care clinicians within three primary modes of treatment: Community Health Centre Model, Fee-for-Service Model, and the Transitional Family Health Network/Team Model. We will document and outline how the nature of the clinical encounter, the capacity to provide consultative services and educational services, and cooperation at the administrative level all vary among these three modes of funding and primary care delivery. The presentation will also include an outline of how to manage and create cooperation to enhance collaborative care in each of the funding models provided.

Objective: How to manage and create cooperation to enhance collaborative care within three differently funded primary care clinics.

Method: Three major primary care clinics currently providing Shared Mental Health Care services were examined for differences in their capacity to engage in the full collaborative process.

Results: Key findings were found in the variation of the clinical encounter, capacity, and cooperation.

Conclusion: This research has the potential to inform other collaborative projects how different funding models impact the collaborative process.

References:

1. Chapter in Book- Addison RB: Doing Qualitative Research, Second Edition, edited by Crabtree BF, Miller WL, Thousand Oaks, Sage Publications Inc, 1999, pp145-161.
2. Book - Kazandjian VA, Lied TR: Health Care Performance Measurement, Systems Design and Evaluation, Milwaukee, WI, Quality Press, 1999.

NR929 Thursday, May 25, 12:00 PM - 2:00 PM

Effectiveness of Aripiprazole Versus Standard of Care: Schizophrenia Trial of Aripiprazole (STAR Trial)

Robert Kerwin, M.D. *London*, Gilbert L'Italien, Ph.D., Linda Hanssens, M.P.H., Ronald N. Marcus, M.D., Robert D. McQuade, Ph.D., Jean-Noel Beuzen, M.D.

Educational Objectives:

To gain an understanding of the utility of effectiveness measures which encompass safety, efficacy, and tolerability in real world practice

Summary:

Background: Naturalistic trials provide an opportunity to assess the overall performance of drugs using measures which encompass efficacy, safety and tolerability (ie effectiveness). We compared the effectiveness at 26 weeks of aripiprazole to standard of care among community treated schizophrenia patients warranting a change in current medication due to tolerability problems and/or suboptimal clinical symptoms control.

Methods: A total of 555 patients were equally randomized to open-label treatment of aripiprazole (10-30 mg/day) or Standard-of-Care (olanzapine 5 - 20 mg/day, or quetiapine 100 - 800 mg/day or risperidone 2 - 8 mg/day, SOC).Overall effectiveness was evaluated using the validated[1] Investigator Assessment Questionnaire (IAQ) Total Score at Week 26 (LOCF). The IAQ Total Score is the sum of 10 items :positive symptoms, negative symptoms, somnolence, weight gain, prolactin elevation, akathisia, EPS, cognition, energy, and mood. Lower scores indicate better effectiveness. Validation studies also showed a good correlation of the IAQ with CGI-I, the preference of medication (POM). Unit decreases in IAQ score correlated with a 20% improvement in the risk of discontinuation[1]. ANOVA was used for all comparisons.

Results: Mean IAQ Total Score at Week 26 was 25.7 ± 0.5 for aripiprazole versus 27.7± 0,5 for SOC p<0.001). Significantly higher CGI-Improvement response ("very much improved" or "much improved") rate was observed at Week 26 in the aripiprazole group (44%) compared with SOC (34%), p=.009 More patients in the aripiprazole group (47%) compared with SOC (29%) rated their study medication as "much better" than prior antipsychotic medication at Week 26 (p<0.001) on the POM scale.

Conclusion: Aripiprazole demonstrated clinically superior effectiveness to SOC in the naturalistic setting of the STAR trial. In real world practice, medication choices should consider efficacy, safety and tolerability issues

References:

1. Tandon R, DeVellis R, Han J, Li H, Frangou S, Dursun S. Validation of the Investigators Assessment Questionnaire, a new clinical tool for relative assessment of response to antipsychotics in patients with schizophrenia and schizoaffective disorder.
2. Guidance on the use of newer (atypical) antipsychotic drugs for the treatment of schizophrenia: National institute for Clinical Excellence;2002.

NR930 Thursday, May 25, 12:00 PM - 2:00 PM

I Can't Be Pregnant! The Phenomena of Denial and Concealment of Pregnancy

Susan J. Hatters-Friedman, M.D. *Case Western Reserve University, Psychiatry, 11100 Euclid Avenue, Hanna Pavilion, Cleveland, OH, 44106*, Amy Heneghan, M.D., Miriam Rosenthal, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognize characteristics associated with denial of pregnancy or concealment of pregnancy. The participant should consider the mental health professional's role in diagnosis and treatment of women with these conditions.

Summary:

This exploratory study sought to comprehensively describe characteristics of women with denial of pregnancy and concealment of pregnancy. Subjects had no prenatal care and presented to our academic medical center either in labor or after delivery, over a seven year period. Sixty-one women with denial of pregnancy and twenty women with concealment of pregnancy were included in the sample. Women had mean ages in their 20s and most noted support from their mothers. Contrary to our hypotheses, most had prior pregnancies, and histories of abuse were not frequently noted.

Women with denial of pregnancy were more likely to be employed, while women with concealment were more likely to be students. Women with concealment of pregnancy experienced awareness of their pregnancy earlier than women with denial of pregnancy.

Surprisingly, psychiatry was rarely consulted, despite sudden and sometimes unexpected childbirth. Almost a third of the mothers were referred to child protective services. The majority of the mothers retained custody of their infants.

Subtypes of both denial and concealment of pregnancy are further delineated in this study. Suggestions for prevention are made.

References:

1. Milden R, Rosenthal MB, Winegardner J, Smith D. Denial of Pregnancy: An Exploratory Investigation. J Psychosom Obstet Gynecol. 1985;4:255-261.
2. Miller LJ: Psychotic denial of pregnancy: phenomenology and clinical management. Hosp Community Psychiatry 1990;41:1233-7.

NR931 Thursday, May 25, 12:00 PM - 2:00 PM

Valproate Treatment of Aggression in Moderate to Severe Alzheimer's Disease

Nathan Herrmann, M.D. *Sunnybrook and Women's College Health Sciences Centre, Psychiatry, 2075 Bayview Ave., Room FG05, Toronto, ON, M4N 3M5, Canada*, Krista L. Lanctot, Ph.D., Goran M. Eryavec, M.D.

Educational Objectives:

At the conclusion of this poster, the participant will recognize that treatment of aggression in Alzheimer's disease with valproic acid is not effective and is associated with an increased incidence of adverse events.

Summary:

Introduction: Aggression is a common serious neuropsychiatric symptom in moderate to severe Alzheimer's disease (AD). Previous studies with valproate therapy have had variable results.

Methods: This was a double-blind randomized placebo-controlled cross-over study in institutionalized AD patients with MMSE scores <15 and Neuropsychiatric Inventory (NPI) agitation/aggression subscale scores ≥ 2. Valproate was initiated at 250 mg/day and titrated up as tolerated to a maximum of 1500 mg/day. The primary outcome measure was the NPI agitation/aggression score.

Results: Fourteen patients (8M/6F), aged 85.57±4.54 years, MMSE 4.50±4.59, NPI agitation/aggression subscale scores 6.43±3.46, were randomized to treatment (all mean±SD). There were 11 (73%) completers; all three noncompleters dropped out during the valproate phase. Average maximum dose of valproate was 1335.55±336.15 mg/day. There was no significant benefit noted on NPI agitation/aggression score. Five of 14 (36%) patients experienced adverse events on placebo and 11 of 14 (79%) on valproate (p=0.001). Mean platelet count decreased significantly with valproate (p=0.032).

Conclusions: Valproate was not an effective treatment for agitation/aggression and was poorly tolerated in this population.

References:

1. Journal Article - Tariot PN, Raman R, Jakimovich L et al: Divalproex sodium in nursing home residents with possible or probable Alzheimer disease complicated by agitation: a randomized, controlled trial. Am J Geriatr Psychiatry 2005; 13:942-959.
2. Journal Article - Porsteinsson AP, Tariot PN, Erb R et al: Placebo-controlled study of divalproex sodium for agitation in dementia. Am J Geriatr Psychiatry 2001; 9:58-66.

NR932 Thursday, May 25, 12:00 PM - 2:00 PM

Self-Mutilation of the Tongue in a Patient With Burning Mouth Syndrome

Alan Hirsch, M.D. *Smell & Taste Treatment and Research Foundation, 845 N. Michigan Ave, Suite 990W, Chicago, IL, 60611*, Haridia Hristea

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the lingual self-mutilation as part of the burning mouth syndrome complex.

Summary:

Objective: Demonstrate self-mutilation as a behavior of burning mouth syndrome (BMS).

Method: Case Study

Results: Self-mutilation of the tongue has been described in a multitude of conditions, but not BMS.

A case is presented in which this behavior is associated with burning mouth syndrome (BMS).

A 49 yo right-handed, married, white woman reported a 12 years history of pain in her mouth, lips and tongue, most intense in the site of a childhood trauma to the lower lip. This pain was unresponsive to numerous medications including Cymbalta, Neurontin, Topomax, Trazadone, Clonazepam, Zonogran, Vicodin, Tylenol with codeine, Prevacid, Medroxyprogesterone, Estodiol and procedures including stellate ganglia blocks and cortisone injections.

Patient admitted that in order to relieve pain, she self-mutilated by using a toenail clipper to cut the fungiform papillae from her tongue. This induced acute pain and bleeding, followed by a brief resolution of the pain. For over a year she cut both sides of her tongue at least once a week. Examination of the tongue revealed cicatrisation, lacerations and secondary microglossia without affecting her speech or swallowing. In response to the perception of her teeth being too sharp, she filed her teeth down with a nail file and sand paper. When instructed to stop this behavior, she switched to daily masticatory self-mutilation of her tongue.

These self-mutilating behaviors represent the patient's attempts to manage her pain.

Conclusion: This case demonstrates that in the assessment and treatment of BMS, self-mutilating behavior should be considered and addressed.

References:

1. van der Ploeg HM, van der Wal N, Eijkman MAJ, et al: Psychological aspects of patients with burning mouth syndrome. Oral Surg 63:664-668, 1987.
2. Grushka M, Sessle BJ: Burning Mouth Syndrome. Dent Clin North Am 35:171-184, 1991.

NR933 Thursday, May 25, 12:00 PM - 2:00 PM

Innovative Teaching Project: Medicine and Cinema

Fabiola Irisarri, Jr., M.D. *La Paz University Hospital.(psychiatry department), atocha 101 4-izq, Madrid, 28012, Spain*, Rut Berdun, M.D., Ana Hospital, M.D., Beatriz Rodriguez Vega, Ph.D., Elena Fernandez-León, M.D., Ignacio Millan, M.D., Marta Morales, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognise the usefulness of the cinema-graphic support in teaching the theory of doctor-patient relationship to medical students.

Summary:

Objectives

This project addresses the necessity to create and develop new capacities and attitudes in Medical students. We believe this could be a way to contribute to the development of the medicine science, as evidence based science as well as a meaning based one.

We prepared the didactic films subject considering that medical students are nowadays and will be in the future immersed in an

audiovisual language. We consider that this language could help to the usual teaching program, by widening their experience

Methods

We filmed two short movies focused on doctor-patient relationship. The first one (4') was about the interaction between a doctor and a patient in a usual medical appointment. We used the experience of two real patients to write this first script. These experiences and movie scenes regarding doctors' points of view and attitudes towards patients were included in the second short movie (20').

Firstly, we showed the first short movie and following this, students filled in a questionnaire regarding doctor and patient's attitudes as well as the evaluation of their relationship. After this, the second film was showed, a discussion about the matter was held and then students were requested to fill in the same questionnaire again. The activity took 90 minutes in each group. The data were analyzed using the SPSS 13.0 program.

Results

Our sample was 108 medical students. Results show a perception and attitude improvement towards patient, overcoat regarding adjectives as *claimant* and *polite*. Doctor's attitude perception fall down. He was evaluated as less effective and encouraging after. Students were able to distinguish different aspects in doctor-patient relationship and to separate this from environmental condition. The activity got a very good evaluation.

Conclusions

The data suggest that cinema can be a meaningful and valuable complementary tool for Medicine and Psychiatry learning and teaching.

References:

1. M. Brownell Anderson: Really Good Stuff. Reports of new ideas in medical education. Annual, peer-reviewed collection of reports on innovative approaches to medical education. Med Educ 2003;37:1025'1049.
2. · Gurpegui J: Colección cine y salud(vol 3) Relaciones y emociones,Zaragoza,imprenta Servicio Aragones de Salud, 2001*.

NR934 Thursday, May 25, 12:00 PM - 2:00 PM

13-Year Interim Results From an International Observational Study of Pregnancy Outcomes Following Exposure to Lamotrigine

Jouko IT Isojarvi, M.D. *GlaxoSmithKline, 3030 Cornwalis Road, Research Triangle Park, NC, 27709*, Marianne Cunnington, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the current risk estimate of major congential malformations in women taking lamotrigine.

Summary:

Objective: To characterize the overall risk of major congentital malformations (MCM) associated with exposure to lamotrigine (LAMICTAL ®).

Methods: Physicians report exposure to lamotrigine during pregnacy and subsequent outcomes on a voluntary basis. Prospective reporting (prior to any knowledge regarding the possible outcome of the pregnancy) early in pregnancy is encouraged. MCMs are classified according to CDC criteria and are reviewed by a pediatrician. The percentage of MCMs is calculated using only prospective first trimester lamotrigine monotherapy and polytherapy exposures. Conclusions are developed and endorsed by a scientific advisory committee.

Results: As of September 2005, 20 MCMs were observed among 707 first trimester monotherapy exposures giving a risk of 2.8% (95% CI 1.8-4.4%). The observed risk among 118 lamotrigine and valproate polytherapy exposures was 11.8% (95% CI 6.8-19.3%). For 256 exposures to polytherapy without valproate, the observed risk was 2.7% (95% CI 1.2-5.8%). The mean and median lamotrigine monotherapy doses for patients with MCMs respectively were 251 and 200 mg/day; the mean and median doses for patients without defects were 281 and 200 mg/day. No consistent pattern of MCM type was observed.

Conclusions: The current data do not indicate any substantial increase in overall risk of MCMs associated with prenatal lamotrigine exposure, though the sample size is insufficient to allow definitive conclusions. The higher frequency of MCMs following lamotrigine-valproate polytherapy is consistent with publications on valproate monotherapy. Continued registration of pregnancies will enhance the statistical power of the study and the data available for physicians to assess the benefit-risk of lamotrigine use in pregnancy.

References:

1. Holmes LB et al. The teratogenicity of anticonvulsant drugs. N Engl J Med 2001;344: 1132'38.
2. Wyszynski DF et al. Increased rate of major malformations in offspring exposed to valproate during pregnancy. Neurology 2005;64:961-965.

NR935 Thursday, May 25, 12:00 PM - 2:00 PM

Catatonia in the Elderly

Vijay Jayanti, B.S. *Neuroscience Alliance, Neuropsychiatry, The Neuroscience Alliance, 330 Taylor Blair Road, West Jefferson, OH, 43162*, Muhammad Aslam, M.D., Jessica Hufford, B.S., Brendan T. Carroll, M.D.

Educational Objectives:

At the conslusion of this presentation, the participant should be able to screen for catatonia in the elderly and identify approaches to diagnosis and treatment. At the conslusion of this presentation, the participant should be able to identify multiple etiologies for medical catatonias in the elderly. At the conslusion of this presentation, the participant should be able to approaches to treatment including bnezodiazepines and electroconvulsive therapy.

Summary:

Objective: Three elderly patients, described in a previous study, suffered major adverse events consequent to the delay in recognizing catatonia at a teaching VA hospital. Since the publication of that cautionary tale, there has been increased awareness of catatonia. Method: We present three cases of catatonia in the elderly from university teaching VA hospitals. Results: A 62 year old man presented with catatonic features and a history of cerebrovascular accident to a neurology service. The initial diagnosis was of Lewy body dementia. However his screening, treatment and outcome support a diagnosis of catatonia due to cerebrovascular disease. A 78 year old man was diagnosed with major depression with psychosis, but was not screened for catatonia. The mental status and catatonia screening exam revealed catatonic signs. After his initial treatment failed, lorazapam was initiated and he returned to his previous level of function. A 69 year old male developed catatonic stupor shortly after medical transfer. He could not tolerate lorazepam due to confusion. Memantine improved his catatonia. Discussion: These three patients had a favorable outcome due to screening, treatment and monitoring. Conclusion: We recommend a screening instrument for catatonia, 2) evaluation for ECT, 3) trial off of benzodiazepines and 4) screening for cerebrovascular disease for suspected cases of catatonia in the elderly.

References:

1. Swartz C, Galang RL. Adverse outcome with delay in identification of catatonia in elderly patients. Am J Geriatr Pyschiatry 2001; 9:78-80.

2. Ungvari GS, Leung CM, Pang AFT, White E. Benzodiazepine Treatment of Catatonia in the Elderly. J Hong Kong Coll Psychiatr 1994; 4: SP2:33-38.

NR936 Thursday, May 25, 12:00 PM - 2:00 PM

What Is the Happiness of the Old?

Changsu Han, M.D. *Ansan City*, Yong-Ku Kim, M.D., Bun-Hee Lee, Seung-Ho Ryu, M.D., Han Yong Jung, M.D.

Educational Objectives:

To know the definition and the conditions of the happiness of the old from their perspectives

Summary:

To know the definition and the conditions of the happiness of the old from their perspectives, we surveyed the 800 Korean old among the subjects who participated to the Ansan Geriatric Depression and Dementia Cohort (AGE) program as a subject. The results of the geriatric depression scale and quality of life scale were also analyzed. The average happiness level of the 706 respondents on the 100 visual analogue scale was 64.7. 128 (18.1%) answered that they are never happy. 168(23.8%) answered that they are most happy when being with their family members. 13.2% answered that they are happy when their family members are alright (economy, health). Other answers were hobby activity (8.1%), being with friends (6.8%), and religious activity (5.8%). The reasons of their unhappiness were poor health condition (28.7%), economic difficulties of their children (14.8%). The level of happiness of the old was significantly different according to their depressive symptoms, and their economic incomes.

References:

1. Stanley M, Cheek J: Well-being and older people: a review of the literature. Can J Occup Ther 2003; 70(1):51-59.
2. Chipperfield JG, Perry RP, Weiner B: Discrete emotions in later life. J Gerontol B Psychol Sci Soc Sci 2003; 58(1):23-34.

NR937 Thursday, May 25, 12:00 PM - 2:00 PM

Differences in Glucose Metabolism Between Responders to Cognitive-Behavior Therapy and Venlafaxine XR in a 16-Week Randomized Controlled Trial

Sidney H. Kennedy, M.D. *UHN, 200 Elizabeth Street, EN8-222, Toronto, ON, M5G 2C4, Canada*, Jakub Z. Konarski, M.S.C., Zindel V. Segal, Ph.D., Roger S. McIntyre, M.D., Helen S. Mayberg, M.D.

Educational Objectives:

To compare changes in brain activity in patients before and after successful treatment of a major depressive episode.

To appreciate differences in brain activity associated with pharmacological versus psychological antidepressant treatment.

Summary:

Background: We have previously reported on changes in glucose metabolism (18-fluoro-deoxyglucose PET - ^{18}FDG-PET) associated with response to disparate antidepressant modalities, including cognitive behavioral therapy, deep brain stimulation, and pharmacotherapy. Herein, we report the changes in ^{18}FDG-PET during a randomized controlled trial of Cognitive-Behavior Therapy versus Venlafaxine XR in treatment responders after 16-weeks.

Methods: Subjects meeting DSM-IV-TR criteria for a Major Depressive Episode in the context of a MDD received an ^{18}FDG-PET scan before randomization and after 16-weeks of either antidepressant treatment with cognitive behavioral therapy (CBT, n=12) or venlafaxine XR treatment (VEN, n=12). Modality specific, and modality-independent, regional brain metabolic changes associated with response to treatment were analyzed.

Results: Response rates were comparable between the Cognitive-Behavior Therapy (7/12) and VEN (8/12) groups. Response to antidepressant treatment in both groups was associated with decreases in glucose metabolism in the orbitofrontal, medial frontal, right dorsolateral prefrontal, and parahippocampal cortices. Increases in the subgenual prefrontal cortex and distinct temporal cortical regions were associated with response to Cognitive-Behavior Therapy, decreases in the left dorsolateral prefrontal cortex and increases in the right caudate metabolism were unique changes to VEN responders.

Conclusions: Treatment of a major depressive episode was associated with decreases in glucose metabolism in distinct prefrontal regions. Consistent with earlier reports, response to Cognitive-Behavior Therapy was associated with a reciprocal modulation of cortical limbic connectivity, while VEN treatment engaged additional cortical and striatal regions previously unobserved by neuroimaging investigations evaluating serotonergic antidepressants' mechanism of action.

References:

1. Goldapple K, Segal Z, Garson C, Lau M, Bieling P, Kennedy S, Mayberg H: Modulation of cortical-limbic pathways in major depression: treatment-specific effects of cognitive behavior therapy. Arch Gen Psychiatry 2004; 61(1):34-41.
2. Seminowicz DA, Mayberg HS, McIntosh AR, Goldapple K, Kennedy S, Segal Z, Rafi-Tari S: Limbic-frontal circuitry in major depression: a path modeling metanalysis. Neuroimage 2004; 22(1):409-418.

NR938 Thursday, May 25, 12:00 PM - 2:00 PM

Predictors of Response to Deep Brain Stimulation for Treatment Resistant Depression

Sidney H. Kennedy, M.D. *UHN, Psychiatry, 200 Elizabeth Street, EN8-222, Toronto, ON, M5G 2C4, Canada*, Kari A. Fulton, B.A., Andres M. Lozano, M.D., Helen S. Mayberg, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to appreciate the impact of predictors of favorable outcome from demographic, symptom, neurocognitive and personality variables on treatment response to DBS.

Summary:

Background: Despite advances in brain research and options for antidepressant treatment, fewer than 50% of patients achieve remission and up to 20% develop treatment resistance. Treatment resistant depression (TRD) is a severely disabling condition for which there are no evidence-based approaches. Deep Brain Stimulation (DBS) is an established safe and effective functional neurosurgery for Parkinson's disease and Essential Tremor (Lozano & Mahant, 1998) combining advances in MRI and precision positioning of stimulation leads.

Objective: Following a preliminary report on the effectiveness of DBS in TRD (Mayberg et al., 2005) the purpose of this study was to identify predictors in an extended who received DBS in anterior cingulate-BA25.

Method: All patients (n = 9) met DSM-IV-TR criteria for MDD. The following baseline variables were examined; Hamilton Rating Scale for Depression (HAMD-17), the Beck Anxiety Inventory, the NEO-Five-Factor Inventory (NEO-FFI) and various demographic, neurocognitive and social support measures.

Results: There was a significant reduction in depression and anxiety scores at 6 months compared to baseline. Six out of the 9 subjects achieved a response. Preliminary analyses suggest

higher baseline HAMD-17 scores and being married was associated with favorable outcome. There was also a trend for the agreeableness domain within the NEO-FFI to predict favorable outcome ($p = 0.06$).

Conclusion: With increasing sample size, it will be important to evaluate baseline predictors of favorable outcome.

References:

1. Lozano AM, Mahant N. Deep brain stimulation surgery for Parkinson's disease: mechanisms and consequences. Parkinsonism Relat Disord 2004;10 Suppl 1:S49-S57.
2. Mayberg HS, Voon V, Lozano HE, McNeely HE, Seminowicz D, Hamani C, Schwalb JM, Kennedy SH. Deep Brain Stimulation for Treatment-Resistant Depression. Neuron 2005; 45: 651-660.

NR939 Thursday, May 25, 12:00 PM - 2:00 PM

A Survey of Psychiatric Inpatients on Service Satisfaction

Seonghwan Kim, Prof. Dr. *Dong-A University Hospital, Psychiatry, 3-1 Dongdaesin-Dong, Seo-Gu, Busan, 602715, Republic of Korea*

Educational Objectives:

Measures of patient satisfaction on health care can provide information on the quality of treatment as well as a customer perspective on continuing treatment and deciding outcome of treatment. Measurement of customer satisfaction in behavioral health services has received increasing emphasis due to clinicians' and researchers' desire to measure outcomes that reflect the patient's unique perspective. Administrators' desire to increase productivity and enhance quality of services is another reason for acceptance of the customer-service perspective.

There are different types of psychiatric facilities, including psychiatric hospitals, general hospitals, and university hospitals in South Korea. The objectives of this study are to compare the inpatient satisfaction with psychiatric services between different type of psychiatric facilities, and assess the relationship between patient satisfaction and sociodemographic and clinical variables in South Korea.

Summary:

Objectives: To compare the inpatient satisfaction with psychiatric services between different type of psychiatric facilities, and assess the relationship between patient satisfaction and sociodemographic and clinical variables.

Methods: An 30-item multidimensional questionnaire which has good validity and reliability was administered to inpatients (n= 348) discharged from psychiatric hospitals, general hospitals, and university hospitals.

Results: Patients discharged from university hospital were significantly satisfied than those of general and psychiatric hospital.

The common items with high percentage of satisfaction were included the attitude and ability of doctor or nurse in all three type of hospitals. But high percentage dissatisfied for the items were different between psychiatric facilities. The patients discharged general and psychiatric hospital expressed high dissatisfaction with the ward rule or environment, but those discharged from university hospital expressed high dissatisfaction with treatment cost and the staff's explanation for hospitalization. Staff attitude is the most important determinant in the satisfaction of psychiatric inpatients.

Sociodemographic variables such as age, gender, marital status, monthly income, education level, employment status, religion were not significantly different in the total scores of satisfaction scale.

But higher satisfaction was associated with more readmissions and longer duration of illness in the psychosis group, with fewer days admitted and fewer readmissions in the neurosis group(anxiety disorder, somatoform disorder, obsessive compulsive disorder), and with longer days admitted in alcoholic group.

Patients with neurosis(anxiety disorder, somatoform disorder, obsessive compulsive disorder) and mood disorder were significantly satisfied than those with psychosis and alcoholic disorder. And patients admitted voluntarily were more significantly satisfied than those admitted involuntarily.

Conclusion: For increasing the satisfaction level of psychiatric inpatient in Korea, University hospital should have concern for the quality of treatment, and both of general and psychiatric hospital make an effort to improve the ward environment.

References:

1. Druss BG, Rosenheck RA, Stolar M: Patient satisfaction and administrative measure as indicators of the quality of mental health care. Psychiatr Serv 1999; 50:1053-1058.
2. Kalman TP: An overview of patient satisfaction with psychiatric treatment. Hosp Community Psychiatry 1983; 34:48-54.

NR940 Thursday, May 25, 12:00 PM - 2:00 PM

Number of Teeth and Incident Dementia in a Korean Community Population

Sung-Wan Kim, M.D. *Chonnam National University Hospital, Psychiatry, 8 Hak-Dong, Dong-Gu, Kwang-Ju, 501-757, Republic of Korea*, Jae-Min Kim, M.D., Il-Seon Shin, M.D., Su-Jin Yang, M.D., Seung-Hyun Lee, M.D., Jin-Sang Yoon, M.D., Hyung-Yung Lee, M.D.

Educational Objectives:

Participants will acknowledge the importance of paying attention to nutritional status in geriatric population for the prevention of dementia.

Summary:

Introduction: Little is known about risk factors for dementia in low income settings. There is growing interest in the role of nutritional factors in dementia which may be particularly important in low income settings. Loss of teeth is an important potential determinant of nutritional status, but has not been investigated as a risk factor for dementia.

Method: 686 community residents in Kwangju, South Korea aged 65 or over were followed over a 2.4 year period and were clinically assessed for incident dementia. Data on number of teeth and use of dentures were obtained as well as self-reported intake of meat, fish and fruits, anthropometric measurements, serum albumin and cholesterol levels.

Results: Fewer teeth were significantly associated with incident dementia, and the association was only apparent in participants without dentures. Strong associations were found between fewer teeth and indices of poor nutrition in this group, although the association with dementia remained significant after adjustment for these and other potential confounding/mediating factors.

Conclusion: Having fewer teeth appears to be a risk factor for dementia and may be explained by adverse nutritional status. Provision of dentures may be a readily available means of modifying this risk in low income settings.

References:

1. Luchsinger JA, Mayeux R: Dietary factors and Alzheimer's disease. Lancet Neurol 2004; 3: 579-587.
2. Shimazaki Y, Soh I, Saito T, et al: Influence of dentition status on physical disability, mental impairment, and mortality in institutionalized elderly people. J Dent Res 2001; 80: 340-345.

NR941 Thursday, May 25, 12:00 PM - 2:00 PM

Compliance of Somatic Disciplines Regarding Psychiatric Consultations

Uwe M. Kinzel, Dr. Med. Sc. *LKH, Knollstrasse 31, 49088 Osnabrueck, 49088, Germany*, Christian Thuberg, Dr. Med. Sc.

Educational Objectives:

At the end of this poster presentation the participant should be able to recognize that somatic disciplines are often not aware of important issues concerning their patients as outlined in psychiatric consultations.

Summary:

The aim of this study was to assess the awareness of somatic disciplines regarding the results of psychiatric consultations.

Methods: We collected several data of all our psychiatric consultations from Oct. 2004 to March 2005. During this period we asked for all the discharge letters to evaluate whether e.g. the psychiatric diagnosis, treatment recommendations and others were cited correctly. Complete data were available for 63 of 181 patients.

Results: Significantly more letters were sent when a psychiatric anamnesis was known. Significantly less letters were written when a patient was diagnosed F0 or F6 or when the reason for the psychiatric consultation was a suicide attempt.

Conclusions: The study shows that severe psychiatric conditions in somatic patients (suicide attempts) do not necessarily lead to special attention in discharge letters from general hospitals, however well known psychiatric conditions as psychiatric anamnesis lead to more attention. Less attention was paid to demented patients, perhaps because of therapeutic nihilism, as well as in personality disorders

References:

1. Rigatelli M, Casolari L, Massari I, Ferrari S :A Follow-Up Study of Psychiatric Consultations in the General Hospital.Psychother Psychosom 2001;70:276-282.
2. Huyse FJ,Herzog T, Lobo A, Malt UF,Oppomeer BC, Stein B,Creed F, Crespo MD,Cardoso G, Guimares-Lopes R, Mayou R,van Moffaert M, Rigatelli M, Sakkas P, Tienari P: European consultation-liaison psychiatric services: The ECLW collaborative study. Acta P.

NR942 Thursday, May 25, 12:00 PM - 2:00 PM

Weight Concerns in Individuals With Body Dysmorphic Disorder

Jennifer E. Kittler, Ph.D. *E.P Bradley Hospital/Brown Medical School, Psychiatry and Human Behavior, E.P. Bradley Hospital, 1011 Veterans Memorial Parkway, East Providence, RI, 02915*, William Menard, B.A., Katharine A. Phillips, M.D.

Educational Objectives:

The educational objectives of this poster are to learn about an underrecognized bodily preoccupation (weight) and associated features in patients with body dysmorphic disorder.

Summary:

Objective: BDD (BDD), a distressing or impairing preoccupation with a non-existent or slight defect in appearance, often focuses on the face or head. It is unclear what proportion of individuals with BDD are preoccupied with their weight, which is a focus of eating disorders and a common concern in the general population. This study determined the prevalence of weight concerns in individuals with BDD, and examined similarities and differences between those with and those without weight concerns. **Method:** 200 BDD subjects were assessed for clinically significant weight concerns. Subjects with weight concerns (in addition to other body area concerns) were compared to those without weight concerns on measures of BDD symptoms, other symptom severity, comorbidity, suicidality, functioning, and quality of life. **Results:** 58 (29.0%; 95% CI=22.7%-35.3%) participants had excessive weight concerns. Participants with weight concerns were younger, more likely to be female, and had more body areas of concern. They also had a higher frequency of certain BDD behaviors, suicide attempts, and comorbidity; greater body image disturbance and depression; and poorer social functioning. **Conclusion:** Weight concerns in BDD deserve further study, as they appear relatively common and are associated with greater symptom severity and psychopathology in several domains.

References:

1. Phillips KA, Menard W, Fay C, Weisberg R: Demographic characteristics, phenomenology, comorbidity, and family history in 200 individuals with body dysmorphic disorder. Psychosom 2005; 46:317-332.
2. Phillips KA: Body dysmorphic disorder. In Treatments of DSM-IV-TR Psychiatric Disorders, edited by Gabbard G, Washington, DC: American Psychiatric Press Inc, in press.

NR943 Thursday, May 25, 12:00 PM - 2:00 PM

OCD Specific Neuropsychological Deficits

Adarsh Kohli *PGIMER, CHANDIGARH, INDIA, deptt. of psychiatry, PGIMER, chandigarh, 160023, India*

Educational Objectives:

The aim of study was to assess specific cognitive deficits using a battery of neuropsychological tests. Twenty-five outpatients with ICD-10 diagnosis of OCD, fulfilling the inclusion criteria were recruited from psychiatry outpatient clinic of the Department of Psychiatry, PGIMER, Chandigarh, INDIA. Twenty-five matched normal controls were recruited. Both groups were administered performance intelligence tests, test for memory, maze learning test, Trail Making Test, perceptual diagnostic test and Wisconsin Card Sorting Test. Detailed neuropsychological profile in terms of mean and SD's of the OCD patients and the normal controls were obtained. There were significant differences on frontal lobe tests (Wisconsin Card Sorting Test and Trail Making Test), subtests of Wechsler Memory Scale and performance test of Wechsler Intelligence Scale. Neuropsychological variables were correlated with the clinical variables (age of onset, duration of illness, and dose of current drug). The implications of the results will be discussed.

Summary:

ABSTRACT

In the recent years evidence has mounted that OCD is a disorder of brain dysfunction associated with distinct patterns of cognitive impairment. The aim of the study was to assess specific cognitive deficits using a battery of neuropsychological tests. Twenty-five outpatients with ICD-10 diagnosis of OCD, of either sex, in the age range of 18-55 years, with at least ten educational years, and stable for at least 3 months prior to assessment were recruited from psychiatry outpatient clinic of the Department of Psychiatry, Post Graduate Institute of Medical Education and Research, Chandigarh, INDIA. Twenty-five normal controls matched on age, education, gender and handedness were recruited as a comparative group. Both the groups were administered a battery of neuropsychological tests comprising of performance intelligence tests, test for memory, maze learning test, Trail Making Test, perceptual diagnostic test and Wisconsin Card Sorting Test. The detailed neuropsychological profile in terms of mean and SD's of the OCD patients and the normal controls were obtained. There were significant differences between the two groups on frontal lobe tests (Wisconsin Card Sorting Test and Trail Making Test), subtests

of Wechsler Memory Scale and performance test of Wechsler Intelligence Scale. Further the neuropsychological variables were correlated with the clinical variables (age of onset, duration of illness, and dose of current drug). The implications of the results will be discussed.

Key words: Neuropsychological, OCD, Cognitive impairment

References:

1. First MB, Spitzer RL, Gibbon M, et al. Structured Clinical interview for axis I DSM-IV Axis I disorders ' Clinician Version (SCID-CV). Washington, DC, American Psychiatric Press, 1997.
2. World Health Organization. The ICD-10 classification of mental and behavioural disorders. Clinical descriptions and diagnostic guidelines. Geneva: WHO, 1992.

NR944 Thursday, May 25, 12:00 PM - 2:00 PM

Intolerance of Uncertainty and Emotional-Oriented Coping

Brian Y. Kong, B.A. *START Clinic, 790 Bay Street, Suite 900, Toronto, ON, M5G 1N8, Canada*, Madalyn Marcus, Leslie Jacobs, Grace Son, Monica Vermani, Martin Katzman

Educational Objectives:

At the conclusion of this presentation, the participant should be able to confirm the potential correlation between the IUS score and less-adaptive coping, thereby demonstrating a possible link between intolerance of uncertainty and less-adaptive emotional-oriented coping strategies. In effect this will lead to an improvement in the assessment and treatment of clinical anxiety disorders.

Summary:

Anxiety disorders have been reported to affect almost 25% of the population, with an estimated cost to the U.S. economy of over $40 billion per year. Hence psychological predictors of anxiety disorder severity have become a source of interest. Psychological factors predictive of the severity of mood and anxiety disorders such as adverse childhood events, and terminal illness have been investigated.

This study involved an assessment of uncertainty in its relationship to coping strategies in patients referred to a tertiary care clinic. Patients received a questionnaire package consisting of several scales assessing different patient variables including the Intolerance of Uncertainty Scale (IUS), and the Coping Inventory for Stressful Situations (CISS). Intolerance of uncertainty has been demonstrated as an important construct involved in worry, and has been suggested as a contributing factor to anxiety disorders such as GAD. The CISS assesses both less-adaptive coping strategies (i.e., emotional-oriented coping), and adaptive coping strategies (i.e., task-oriented coping). Less-adaptive coping strategies have been associated with less-adaptive personality traits and psychological distress, while adaptive coping strategies have been associated with adaptive personality traits and lack of distress.

We hypothesized that the scores of the IUS and CISS emotional-oriented subscale would produce a positive correlation. Our preliminary data (N=12) have indicated a significant correlation of .737 (p-value .006) between the scores of the IUS and CISS emotional-oriented subscale. It is predicted that upon further collection of data, we will be able to confirm the potential correlation between the IUS score and less-adaptive coping, thereby demonstrating a possible link between intolerance of uncertainty and less-adaptive emotional-oriented coping strategies.

References:

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2. McWilliams LA, Cox BJ, Enns MW. Use of the Coping Inventory for Stressful Situations in a clinically depressed sample: factor structure, personality correlates, and prediction of distress. J Clin Psychol 2003; 59:423-37.

NR945 Thursday, May 25, 12:00 PM - 2:00 PM

The Effects of Depression and Anxiety on Neuropsychological Performance in Mild Traumatic Brain Injury

Terry Lee-Wilk, Ph.D. *University of Maryland School of Medicine, 460 Lynette St., Gaithersburg, MD, 20878*, Robert L. Kane, Ph.D., Jack Spector, Ph.D., Karen Murdock, M.S., Joseph Kufera, M.S., Kimberly Auman, M.S., Patricia Dischinger, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the effects of depression and anxiety on measures of neuropsychological functioning in a sample of participants with mild traumatic brain injury.

Summary:

Objective: To assess the effects of depression and anxiety on measures of neuropsychological functioning in a sample of participants with mild traumatic brain injury (mTBI).

Methods: Forty-six participants, ages 18-64, with mTBI (Glasgow Coma Scale 13-15) admitted to an emergency room of an urban hospital were included in this longitudinal study. Participants were asked to report depression and anxiety symptoms as part of a clinical interview, using the Well-Being Scale, 3-months post injury. Participants were also assessed with the Automated Neuropsychological Assessment Metrics (ANAM), a computerized library of tests designed to serially assess neuropsychological functioning. To reduce the number of variables, several tests were combined into a weighted composite. In addition, measures of simple (sRT) and choice (pRT) reaction time were measured.

Results: Results of regression analyses adjusted for age, gender, education, and S100B (a biological serum marker of astroglial cell death representative of CNS damage) indicated no significant effects of 1) *depression* on the three outcomes (p=0.44-0.66); 2) *anxiety* on the three outcomes (p=0.37-0.44); or 3) *depression and anxiety* on the three outcomes (p=0.40-0.48).

Conclusions: Findings from previous literature have consistently documented the association between mild TBI and symptoms of depression and anxiety. However, the literature is mixed regarding the effects of depression and anxiety on performance of neuropsychological measures in mild TBI samples. These findings suggest no effects of depression and/or anxiety on measures of Sustained Release T, pRT, or overall neuropsychological functioning. Although depression and anxiety are commonly associated with mild head injury, it does not mediate deficits observed on measures of neuropsychological functioning in this sample.

References:

1. Rapoport MJ, McCullagh S, Shammi P, Feinstein A: Cognitive impairment associated with major depression following mild and moderate traumatic brain injury. J Neuropsychiatry Clin Neurosci 2005; 17:61-65.
2. Suhr JA, Gunstad J: Further exploration of the effect of "diagnosis threat" on cognitive performance in individuals with mild head injury. J Int Neuropsychol Soc 2005;11:23-29.

NR946 Thursday, May 25, 12:00 PM - 2:00 PM

Physical and Psychosocial Factors Relating to Medical Outcomes in Early Inflammatory Arthritis

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Catherin, Montreal, PQ, H3T 1E2, Canada, Murray Baron, M.D., Margaret Purden, Ph.D., Orit Scheir, B.A., Phyllis Zelkowitz, Ed.D.

Educational Objectives:

At the conslusion of this presentation, the participant should be able to:

1. be aware of the importance of psychosocial factors in outcomes of early inflammatory arthritis.
2. understand a model of the relationship among sociodemographic variables, depressive symptoms and disease outcomes in early inflammatory arthritis.
3. identify potential areas of intervention that may improve physical and global health of patients with early inflammatory arthritis.

Summary:

Introduction: Inflammatory Arthritis is a disease consisting of joint inflammation leading to pain, tissue damage, deformity, and disability. This study investigates the relationship among sociodemographic variables, depressive symptoms, and disease outcomes in patients with new-onset inflammatory arthritis.

Methods: The sample consists of 122 patients with early inflammatory arthritis (EIA) (> 1 swollen joint, duration > 6 weeks & < 1 year, no specific diagnosis other than rheumatoid arthritis) who underwent a physical assessment and completed self-report questionnaires including the Center for Epidemiological Studies Depression scale (CESD), McGill Pain Questionnaire (MPQ), the Stanford Health Assessment Questionnaire Disability Index (HAQ-DI), and World Health Organization Disability Assessement Schedule II (WHODAS II).

Results: Income, level of education, number of people living at home, and number of swollen joints were correlated with CESD on bivariate analysis, but only income and number of swollen joints remained significantly associated with CESD in multivariate analysis. In multivariate models of disease outcomes (pain, physical functioning, quality of life), the CESD and swollen joints were significantly associated with pain (MPQ) and physical functioning (HAQ-DI), while CESD and income were significantly associated with quality of life (WHODAS II).

Conclusions: This study identifies physical and psychosocial factors relating to disease outcomes in new-onset inflammatory arthritis. The number of swollen joints predicted depression, pain, and level of physical functioning. Level of income predicted depression and quality of life. Depression had the most consistent relationship with disease outcomes, contributing to multivariate models of pain, physical functioning, and quality of life in patients with EIA. The results of this study suggest that addressing financial and emotional factors in EIA in addition to the physical manifestations of the disease may have a beneficial effect on multiple disease outcomes.

References:

1. Escalante A, del Rincon I: How much disability in rheumatoid arthritis is explained by rheumatoid arthritis? Arthritis Rheum 1999;42:1712-21.
2. Holm MB, Rogers JC, Kwoh CK. Predictors of functional disability in patients with rheumatoid arthritis. Arthritis Care Res 1998;11:346-55.

NR947 Thursday, May 25, 12:00 PM - 2:00 PM

Differences Between Spiritist Mediumship and DID on Structured Interview

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Educational Objectives:

At the conclusion of this presentation, the participant should have better knowledge to make an adequate differential diagnosis between dissociative identity disorder and experiences regarded as mediumistics.

Summary:

Objectives: To study for similarities and differences between spiritistic mediums and DID patients based on a structured interview.

Methods: Twenty four mediums, selected among different spiritist organizations in Sao Paulo, Brazil were interviewed by using the Dissociative Disorder Interview Schedule, and the results were compared with DID symptoms described in the literature.

Results: The spiritist mediums are similar to the DID patients with respect to female prevalence (76.5%), high frequency of Schneiderian First-Rank Symptoms of Schizophrenia (average of 4 per medium) and reports of extrasensory experiences. Meanwhile, the mediums deviate in other characteristics: better social adjustment, low prevalence of mental disorder, lower use of mental health services, no use of antipsychotics, lower prevalence of histories of both physical (8.3%) and sexual (21.7%) childhood abuse, sleepwalking (20.8%), imaginary childhood playmates (25%), secondary features of DID (average of 2.2) and symptoms of BPD (average of 1.2).

Conclusion: The mediumistic experiences analyzed seem to not be comparable to DID since the former are associated with better mental health, social adjustment and differ in almost all DID clinical characteristics.

This study was supported by a grant from the FAPESP (The State of São Paulo Research Foundation), grant no.01/02298-0.

References:

1. Cardeña E, Lewis-Fernández R, Bear D, Pakianathan I, Spiegel D: Dissociative Disorders. In DSM-IV Sourcebook, American Psychiatric Association, Washington, DC, American Psychiatric Press, 1994.
2. Ross CA, Miller SD, Reagor P, Bjornson L, Fraser GA, Anderson G: Structured Interview Data of Multiple Personality Disorder from Four Centers. Am J Psychiatry 1990; 147: 596-601.

NR948 Thursday, May 25, 12:00 PM - 2:00 PM

Assessing the Brain Reward System in Alzheimer's Disease Using Dextroamphetamine Challenge: Relationship With Apathy

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Educational Objectives:

At the conclusion of this poster, the participant will be able to (1) understand the use of dextroamphetamine as a probe of the dopaminergic brain reward system and (2) recognize the potential role of dysfunction of the brain reward system in apathy associated wiht Alzheimer's disease.

Summary:

Background: Apathy is among the most common neuropsychiatric symptoms in Alzheimer's disease (AD). Our goal was to assess the dopaminergic pathways of the brain reward system (BRS) in apathetic versus non-apathetic patients.

Methods: A single oral dose of dextroamphetamine (d-amph; 10 mg) was used to release dopamine and probe the activity of the BRS. Subjective, behavioural, and physiological measures were recorded at baseline and at hourly intervals post-d-amph in

apathetic and non-apathetic AD patients. Drug rewarding effects were assessed with the Addiction Research Centre Inventory (ARCI), current mood was assessed with the Profile of Mood States (POMS), and attention was assessed with the CPT.

Results: Of 21 (12M/9F), elderly (age 78± 8 years), nondepressed (NPI depression=0) patients with mild dementia (MMSE 18.64±3.91), 14 were apathetic (NPI apathy score range 2-12). Demographics characteristics, including age, gender, and MMSE were similar in the apathetic and non-apathetic groups (all p>0.05). Subjective rewarding d-amph effects increased in both groups. ANCOVA with peak effect as the dependant variable, apathy as the between-subjects factor and baseline scores as a covariate showed significant differences in ARCI positive effects (p=.024), POMS rewarding effects (p<.001), CPT attention (p<.001), CPT impulsivity (p=.01) and CPT vigilance (p=.001) with no significant changes in negative effects (p=.09). Of these, only ARCI positive effects composite showed a trend for a difference by apathy group (p=.056), with all others showing baseline differences (all p<.05). A significant negative correlation between apathy severity (Apathy Evaluation Scale) and d-amph rewarding effects (ARCI positive effect composite: r=-0.43, p=.05) was found.

Conclusions: These preliminary results suggest apathy may be associated with a decrease in rewarding effects of an amphetamine probe. The ability to respond to amphetamine with characteristic changes implies that the dopaminergic system may be a feasible target for pharmacotherapy in early dementia.

References:

1. Journal Article - Moosa S, Lanctôt KL, Herrmann N, et al. Neuroanatomical correlates of apathy associated with Alzheimer's disease by means of statistical parametric mapping. Annals of Neurology 2004; 56 (suppl 8): S66.
2. Journal Article - Tremblay LK, Naranjo CA, Cardenas L, Herrmann N, Busto UE: Probing brain reward system function in major depressive disorder: altered response to dextroamphetamine. Arch Gen Psychiatry 2002; 59(5): 409-16.

NR949 Thursday, May 25, 12:00 PM - 2:00 PM

The Relationship of Psychiatric Disorders, Diabetes, and Diabetic Peripheral Neuropathy to Pain in Primary Care Patients

Kathryn Magruder *Medical University of South Carolina, 67 President Street, Post Office 250861, Charleston, SC, 29425,* D. E. Yeager, M. A. Timmerman, D. E. Clancy, Rebecca Robinson

Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand the relationship between self-reported pain and diabetes, diabetic peripheral neuropathy, and psychiatric diagnoses for VA patients in primary care settings. The relationship between health services use and pain medication use will also be addressed.

Summary:

Objective: To examine the contribution of psychiatric disorders, diabetes, and diabetic peripheral neuropathy (DPN) to patients' assessment of pain.

Method: Patients were randomly selected (oversampling women) from primary care clinics at four VA hospitals. Sociodemographic characteristics and functional status were collected using the SF-36, including 2 items of bodily pain (SF-BP). Using the median pain score (62.5) patients were classified as having "more pain" or "less pain". The electronic medical record provided ICD-9 diagnoses for a 2-year period with interview date as the midpoint.

Results: 73% (n=938) of invited patients consented and had complete data. 32.7% of patients were diabetic, 10.2% of whom had DPN; 41.3% had a psychiatric diagnosis (23.8% major depression or depression NOS; 9.5% PTSD). Pain scores indicated more pain than published normative data on patients with either diabetes or depression. In a logistic regression analysis with diabetes, DPN, depression, PTSD, age, sex, and race in the model, only depression (OR=2.56; 1.81-3.61), PTSD (OR=3.16; 1.81-5.54), and being female (OR=.68; .47-.99) were significantly (p<.05) associated with higher levels of pain.

Conclusions: Patients with psychiatric diagnoses are more likely to report higher levels of pain regardless of a diagnosis of diabetes or DPN.

This research was funded by Eli Lilly.

References:

1. Bair MJ, Robinson RL, Katon W, Kroenke K. Depression and pain comorbidity. A literature review. Arch Int Med 2003;163:2433-2445.
2. de Groot M, Anderson R, Freedland KE, Clouse RE, Lustman PJ. Association of depression and diabetes complications: a meta-analysis. Psychosom Med 2001; 63(4):619-630.

NR950 Thursday, May 25, 12:00 PM - 2:00 PM

Toward a Rehabilitative Model of Care Through an Academic State Hospital Collaboration: Change Over Two Years

David I. Mayerhoff, M.D. *1)Greystone Park Psychiatric Hospital. 2)UMDNJ, Psychiatry, 50 Ellis Drive, Greystone Park Psychiatric Hospital, Greystone Park, NJ, 07950,* Jeffry Nurenberg, M.D., Russell Smith, M.S., Steven J. Schleifer, M.D., Marlene Morris, R.N.

Educational Objectives:

At the conclusion of the session, participants should be able to

1. better understand State Hospital - University collaborations as a vehicle for institutional change.
2. recognize and better appreciate the role of rehabilitative interventions and assessment of novel behavioral dimensions as tools for shifting to a recovery oriented model in State Hospital settings.
3. demonstrate the application of a novel scale to assess intrusiveness in a clinical setting and understand the underlying relevance of this scale to patient care.

Summary:

Objectives: State hospitals are shifting focus from symptom control to rehabilitation/recovery through programming and attitudinal change. Our multidisciplinary State-University affiliation collaborated on such a program on a 20-bed unit with extended stay patients. Methods: From August, 2003, university/hospital teams focused on therapeutic communication, crisis response and team building. Psycho-education used the Liberman Re-entry Model and Team Solutions. Programming addressed practical barriers to community living. Among others, the Ward Atmosphere scale and a novel scale measuring patient intrusiveness/InYourFace behavior (IYF) were used.

Results/Observations: During the first 18 months, recovery-oriented interventions became more evident, with improved rapport and problem solving. 4/10 readiness-group participants (November, 2004) were discharged within 7 months, others showed increased recovery-orientation. Discharges increased 50% in year two, as Ward Atmosphere (Moos S) improved (F=15.2; p<0.0001), especially patient independence and treatment acceptance. Staff-perceived IYF decreased progressively (2005 versus 2003: F=4.1; p=.052), unrelated to overt aggression levels. Change appeared to reflect ward atmosphere and evolving administrative policy restricting patients with severe (albeit nonviolent) character pathol-

ogy. The latter, assessed clinically, predicted IYF in multiple regression (t=3.4; p<0.002). Observations from a novel (for hospitals) Illness Management and Recovery initiative are pending. The program suggests that substantial reorientation on a typical state hospital unit can be effected over 2 years.

References:

1. Moos RH. Evaluating treatment environments. New Brunswick, NJ, Transaction Publishers, 2nd Edition, 1996.

2. Meuser KT, Corrigan PW, Hilton DW, Tanzman B, Schaub A. Gingerich S, Essock SM, Tarrier N, Morey B, Vogel-Scibilia S. Illness, Management and Recovery. A Review of the Research. Psychiatric Services 53, 1272-1284, 2002.

NR951 Thursday, May 25, 12:00 PM - 2:00 PM

Evacuation of SMI Veterans During Natural Disasters

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Educational Objectives:

At the conclusion of this presentation, the participant should have a better understanding of what is needed for a successful evacuation of SMI patients.

Summary:

Objective: Recent hurricanes forced evacuation from two VISN16 locations in Mississippi and Louisiana. Evacuations were planned with no precedence for seriously mentally ill (SMI) persons. A plan for mental health professionals/disaster teams on issues pertaining to effective evacuation of (SMI) persons is proposed.

Methods: Three teams were deployed by the CAVHS Mental Health Service and the MIRECC clinical director to evacuate forty SMI veterans from inpatient and residential care settings in Biloxi, MS and Alexandria, LA. Teams consisted of psychiatrists, psychiatric residents, nurses, social workers, and LPNs.

Results: Clinical information for evacuees' was not available. Most patients were not informed of the move to another facility until approached by the evacuating team. While most evacuating patients seemed to understand and cooperated despite their psychotic disorder, some required education and medications to ensure safe transfer. Evacuation teams anticipated needs of the SMI patients and carried medications, food, supplies and members of a variety of disciplines to assist with safe and expeditious evacuations.

Conclusions: We offer recommendations to prepare teams to meet the needs of SMI evacuees. Evacuation teams should be multidisciplinary although size depends on the evacuee population. Clinician communication is critical and evacuees should be informed of the situation prior to evacuation. If medical records are computerized and linked, as with the VA, identification of patients to be evacuated should be relayed to the evacuating team early. The transferring facility should prepare patients, inform their next of kin, if possible, and arrange routine medications for the journey. Supplies should include sanitation and hygiene products, food, drinks, and a medication chest. With an aging veteran SMI population, the team needs be ready to meet routine needs and arrange emergency treatment for acute medical care during transfer.

Impact: Disaster response teams should prepare to specifically meet the needs of SMIs.

NR952 Thursday, May 25, 12:00 PM - 2:00 PM

Obesity and Mood Disorders: Results From a National Community Health Survey on Mental Health and Well Being

Roger S. McIntyre, M.D. *University Health Network, Mood Disorders Psychopharmacology Unit, 399 Bathurst Street, MP-9-325, Toronto, ON, M5T 2S8, Canada*, Jakub Z. Konarski, M.S.C., Kathryn Wilkins, M.S.C., Sidney H. Kennedy, M.D.

Educational Objectives:

1. Employ a population-based investigation to simultaneously estimate the prevalence of obesity in both bipolar disorder and major depressive disorder.
2. Evaluate the hypothesis that indices of excess weight are relatively more prevalent in persons screening positive for a major depressive or manic episode.
3. Examine factors that may moderate the obesity-mood disorder covariation.

Summary:

Objectives: We aimed to ascertain the prevalence of obesity in people with a mood disorder (MD) (bipolar disorder or MDD) compared to the general population. A further aim was to examine the likelihood of an obesity-MD association whilst controlling for the influence of sociodemographic variables.

Methods: The analysis was based on data from Statistics Canada's Canadian Community Health Survey: Mental Health and Well-being (CCHS), conducted in 2002. The sample (n=36,984; ≥15 years old) was drawn from the household-dwelling population of Canada; the CCHS used diagnostic criteria outlined in the DSM-IV-TR to screen respondents.

Results: Persons with a lifetime history of MD were more likely to be obese (19% versus 15%, respectively (p<0.001), and morbidly obese [Body Mass Index ≥40], 2% versus 1%, respectively (p<0.01). In sex-specific multivariate analysis, lifetime MD was associated with elevated odds of obesity in women (OR=1.22; 95% CI=1.03-1.46), but not in men. Antipsychotic pharmacotherapy was also associated with obesity.

Conclusions: This is the first Canadian epidemiological investigation to specifically evaluate anthropometric indices and associated factors in the MD population. The results herein supplement substantial clinical evidence documenting the association between mood disorders and stress-sensitive somatic disorders (e.g., obesity). These data also underscore the metabolic consequences of some psychotropic agents.

References:

1. Fagiolini A, Kupfer DJ, Houck PR, Novick DM, Frank E: Obesity as a correlate of outcome in patients with bipolar I disorder. Am J Psychiatry 2003; 160(1):112-117.

2. McElroy SL, Kotwal R, Malhotra S, Nelson EB, Keck PE, Nemeroff CB: Are mood disorders and obesity related? A review for the mental health professional. J Clin Psychiatry 2004; 65(5):634-51,.

NR953 Thursday, May 25, 12:00 PM - 2:00 PM

Medical Comorbidity in Bipolar Disorder: Implications for Functional Outcomes and Health-Service Utilization

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Educational Objectives:

To ascertain the prevalence and functional/medical service utilization implications of comorbid general medical disorders in persons screening positive for bipolar disorder.

Summary:

Background: This is the first cross-national population-based investigation which aims to ascertain the prevalence and functional/medical service utilization implications of comorbid general medical disorders in persons screening positive for bipolar disorder (BD).

Methods: Data were extracted and analyzed from the Canadian Community Health Survey: Mental Health and Well-Being (CCHS). Cross-sectional associations between lifetime WHO-CIDI-defined manic episode and selected chronic conditions were examined; effects of a manic episode and medical comorbidity on functional outcomes are reported. Respondents (n=36,984) to the survey were aged 15 or older. The sample was drawn from the household-dwelling population of the ten provinces; the data are weighted to be representative of this population. Respondents were also asked about concurrent physician-diagnosed chronic medical disorders, sociodemographics, interpersonal/social functioning, workplace disability/ compensation and medical service utilization.

Results: An estimated 589,000 (2.4%) persons met criteria for BD based on screening positive for a lifetime manic episode. Persons who screened positive for BD had a relatively higher prevalence of chronic fatigue syndrome (3.8% versus 1.1%; p< 0.05),, migraine (24.8% versus 10.3%; p<0.05), asthma (15.9% versus 8.3%; p<0.05), chronic bronchitis (7.9% versus 3.1%; p<0.05), multiple chemical sensitivities (4.6% versus 2.3%; p<0.05), and gastric ulcer (10.9% versus 3.9%; p<0.05).The presence of a comorbid chronic medical disorder was associated with a more severe course of BD illness as indicated by household/ work maladjustment, disability payments, reduced education/employment, and more frequent medical service utilization.

Conclusions: Comorbid medical disorders among bipolar persons are associated with harmful dysfunction, decrements in functional outcomes, and increased medical-service utilization.

References:

1. Osby U, Brandt L, Correia N, Ekbom A, Sparen P: Excess mortality in bipolar and unipolar disorder in Sweden. Arch Gen Psychiatry 2001; 58(9):844-850.

2. Kessler R: Comorbidity of unipolar and bipolar depression with other psychiatric disorders in a general population survey., in Comorbidity in Affective Disorders. Edited by Tohen M. New York, Marcel Dekker Inc., 1999, pp 1-25.

NR954 Thursday, May 25, 12:00 PM - 2:00 PM

The Prevalence and Impact of Migraine Headache in Bipolar Disorder: Results From the Canadian Community Health Survey

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Educational Objectives:

To report on the prevalence of comorbid migraine in bipolar disorder and the implications for bipolar age of onset, psychiatric comorbidity, illness course, functional outcome and medical service utilization.

Summary:

Background: Migraine comorbidity is differentially reported in bipolar versus unipolar depressed clinical samples. The bipolar disorder-migraine association and its consequences has been infrequently reported in epidemiological studies.

Methods: The prevalence of comorbid migraine in bipolar disorder (BD) and the implications for BD age of onset, psychiatric comorbidity, illness course, functional outcome and medical service utilization were evaluated from respondents (n=36 984) to the Canadian Community Health Survey: Mental Health and Well-Being (CCHS). Respondents reporting a lifetime WHO-CIDI-defined manic episode and physician diagnosed migraine (lifetime) were compared to respondents without migraine on sociodemography, course of illness, and medical service utilization indices.

Results: An estimated 2.4% of the sample met criteria for BD. Persons with BD had a relatively higher prevalence of migraine versus the general population (24.8% versus 10.3%; p<0.05). The sex-specific prevalence of comorbid migraine in BD was, 14.9% for males and 34.7% for females. Bipolar males with comorbid migraine were more likely to live in a low income household (p< 0.05); receive welfare and social assistance (p< 0.05); report an earlier age of onset of BD (p< 0.05); have a higher lifetime prevalence of comorbid anxiety disorders (p< 0.05). Bipolar males with comorbid migraine were also more likely to utilize primary (p< 0.05) and mental health care services (p< 0.05), and a trend towards contact with a physician (p=0.09). Bipolar females with comorbid migraine had more comorbid medical disorders (p< 0.05) and required help with personal or IADLs when compared to bipolar females without migraine.

Conclusion: Bipolar disorder with comorbid migraine is prevalent and associated with greater dysfunction and medical service utilization, notable in males. Opportunistic screening and surveillance for bipolar and comorbid migraine is warranted.

References:

1. Low NC, Du Fort GG, Cervantes P: Prevalence, clinical correlates, and treatment of migraine in bipolar disorder. Headache 2003; 43(9):940-949.

2. Mahmood T, Silverstone T, Connor R, Herbison P: Sumatriptan challenge in bipolar patients with and without migraine: a neuroendocrine study of 5-HT1D receptor function. Int Clin Psychopharmacol 2002; 17(1):33-36.

NR955 Thursday, May 25, 12:00 PM - 2:00 PM

The Regulation of Negative Affect and BPD: Study Using Ecological Momentary Assessment

Lauren B. McSweeney *McLean Hospital, 115 Mill St, Service 125, Belmont, MA, 02478*, Mary C. Zanarini, Katherine M. Putnam

Educational Objectives:

At the conclusion of this presentation, the participant should be able to identify which aspects of emotion regulation lead to increased negative affect (NA) in individuals with borderline personality disorder (BPD).

Summary:

Objective: Deficits in emotion regulation have been observed in BPD and are considered to influence the presentation of other symptoms observed in the disorder (Skodol et al, 2002). One mechanism for this may be through the inability to down-regulate intense negative affect (NA). This report is part of a larger study examining the neurophysiology and self-report of emotion dysregulation in BPD. Here, we report on the phenomenology of emotional experience in BPD and its relationship to scales known to measure emotion dysregulation. Methods: Thirteen female college students met criteria for BPD with the DIB-R (Zanarini et al.,

1989) and the DIPD-IV (Zanarini et al., 1996). Current mood was assessed by repeated, longitudinal assessments (Ecological Momentary Assessment; EMA) 8 times daily for 5 days; several questionnaires were administered that tap different aspects of emotion dysregulation (Response Style Questionnaire (Nolen-Hoeksema & Morrow, 1991), the Emotion Regulation Questionnaire (Gross & John, 2003), Emotion Regulation Scale (Jackson & Davidson, unpublished)). Results: In order to examine the relationships between these measures, we utilized a mixed level linear model and found that NA was positively predicted by aspects of emotion dysregulation (all p's<0.05). Conclusions: These results indicate that in BPD, deficits in the ability to regulate affect are linked to reports of increased NA experienced in daily life.

References:

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NR956 Thursday, May 25, 12:00 PM - 2:00 PM

Predictive Power of Childhood Sexual Abuse Parameters to Time-to-Remission in Individuals With BPD

Lauren B. McSweeney *McLean Hospital, 115 Mill St, Service 125, Belmont, MA, 02478*, Mary C. Zanarini, Frances R. Frankenburg, D. Bradford Reich, Kenneth R. Silk

Educational Objectives:

At the conclusion of this presentation, the participant should be able to identify which parameters of childhood sexual abuse (CSA) predict time-to-remission from borderline personality disorder (BPD).

Summary:

Objective: This study explored the relationship of specific abuse parameters to time-to remission from BPD. Methods: A group of 290 inpatients met criteria for BPD with the DIB-R (Zanarini et al., 1989) and the DIPD-IV (Zanarini et al., 1996). Overall, 62.4 % of borderline patients (181 of 290) retrospectively reported a childhood history of sexual abuse on the Abuse History Interview (AHI; Zanarini et al., 1999). In carrying out the time-to remission analyses, we first assessed the relationship between each of the six childhood sexual abuse (CSA) predictor variables (as assessed in the AHI) and time-to-remission, while controlling for baseline severity of borderline pathology (as assessed by the total score of the DIB-R). Remission was defined as no longer meeting either of our study criteria sets for BPD (DIB-R and DSM-III-R). Results: Univariate analyses revealed four significant CSA predictor parameters: multiple perpetrators, penetration, ongoing abuse and duration of abuse. Mulitvariate analyses revealed penetration was the most powerful CSA parameter to predict time-to remission from BPD. Conclusions: Reported sexual penetration seems to slow remission from BPD.

References:

1. Zanarini, M.C., Yong, L., Frankburg, F.R., Hennen, J., Reich, D.B., Marino, M.F., & Vujanovic A. A. (2002). Severity of reported childhood sexual abuse and its relationship to severity of borderline psychopathology and psychosocial impairments among.
2. Silk, K.R., Lee, S., Hill, E.M., & Lohr, N. (1995). Borderline personality disorder symptoms and severity of sexual abuse. Am J Psychiatry, 152, 1059-1064.

NR957 Thursday, May 25, 12:00 PM - 2:00 PM

Psychopathological and Neuropsychological Profile of 100 Consecutive Adult Cases of Delirium

David J. Meagher *Regional Hospital, Dooradoyle, Limerick, Ireland*, Bangaru Raju, Maria Moran, Sinead Donnelly, Dympna Gibbons, Paula Trzepacz

Educational Objectives:

To decribe the phenomenological profile of delirium in greater detail than previous work and to explore how cognitive and non-cognitive symptoms inter-relate

Summary:

Background: Delirium phenomenology is understudied. We investigated the frequency and interrelationship of a range of cognitive and non-cognitive delirium symptoms using standardized scales.

Method : Consecutive cases of delirium were identified in a palliative care setting using the Confusion Assessment Method (CAM) and DSM-IV criteria. Symptom profile was assessed using the Delirium Rating Scale-Revised-98 (DRS-R98) and Cognitive Test for Delirium (CTD).

Results : The 100 patients [50 male, mean age 70.1±11.5, mean etiological categories per case 3.5 ± 1.3, mean DRS-R98 Severity score 16.6 ± 5.5, mean CTD score 14.5 ± 8.1] had a wide range of symptoms with highest incidence of sleep-wake cycle abnormalities (97%), motoric disturbance (94%), and inattention (97%). Patients with psychotic symptoms (n=49) had either perceptual disturbances or delusions but rarely both. Thought disturbance but not delusions or hallucinations, was linked to cognitive impairments. Cognitive items measured on the CTD and DRS-R98 were closely correlated despite their differing time frames. The level of inattention was closely linked to all other cognitive disturbances on the DRS-R98 and CTD but not to non-cognitive features of the DRS-R98. Comprehension was the cognitive item that related most closely to non-cognitive features of delirium. Ward management difficulties correlated with agitation, affective lability and overall severity of delirium.

Conclusions : Delirium is a complex neuropsychiatric disorder characterised by inattention as well as disturbances of other cognitive domains, sleep-wake cycle disturbances and motor activity alterations. Attention and comprehension together are the cognitive items that best account for the syndrome of delirium. The degree of fluctuation of many delirium symptoms, especially cognitive impairments, may not be as great as previously thought. Psychosis in delirium differs from that in dementia and functional psychoses.

References:

1. Meagher DJ, Trzepacz PT (1998). Delirium phenomenology illuminates pathophysiology, management, and course. J Ger Psych Neurol 11:150-156.
2. Francis J (1995). A half-century of delirium research: time to close the gap. JAGS 43:585-6.

NR958 Thursday, May 25, 12:00 PM - 2:00 PM

Motoric Symptoms and Subtypes in 100 Cases of Adult Delirium

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Educational Objectives:

To explore the frequency and relevance of motoric disturbances to the syndrome of delirium. To investigate the degree of concordance between existing approaches to motoric subtyping of delirium

Summary:

Background: Motorically defined subtypes of delirium may have clinically significant differences but descriptions have included non-motoric symptoms and different schema have not been compared in the same sample. We prospectively studied delirious patients using 4 different methods for defining psychomotoric subtypes.

Method: Unique items from three different schema were merged to form a new 30-item Delirium Motoric Checklist (DMC) to collect data that could then be used to both assess phenomenology and rate each schema. Motoric symptom profile was compared between 100 patients with DSM IV delirium and 52 non-delirious controls. The DRS-R-98 was used to assess for strength of association to its two motoric items.

Results: Patients were half male, mean age was 70.1 ± 11.5 years, mean DRS-R98 Severity scores were 16.6 ± 5.5 consistent with mild to moderate delirium. Psychomotoric symptoms were more common in delirious patients with 18 DMC items (60%) significantly more frequent compared to controls. With Bonferroni correction for multiple comparisons, 8 hyperactive and 3 hypoactive DMC items distinguished delirium cases from controls. The frequency of motoric subtypes varied considerably across the 4 subtyping methods (Hyperactive 20-37%; Hypoactive 11-31%; Mixed 28-64%; None 4-19%). Concordance among the 4 subtyping methods was only 34% and rates between any two schema ranged from 48 to 76%. The DRS-R98 identified about twice as many hypoactive cases compared to the other three methods and the Lipowski schema identified the most mixed subtypes.

Conclusions: Motoric disturbances are a frequent component of delirium and need to be better represented in diagnostic criteria. Current approaches to motoric subtyping include symptoms unrelated to motoric behaviour, items that lack specificity for delirium, and lack consistency across schema

References:

1. Meagher DJ, Trzepacz PT (2000). Motoric subtypes of delirium. Sem Clin Neuropsychiatry 5:75-85.
2. Liptzin B, Levkoff SE (1992). An empirical study of delirium subtypes. Br J Psychiatry 161:843-5.

NR959 Thursday, May 25, 12:00 PM - 2:00 PM

Cost-Effectiveness of Atypical Antipsychotics in the Treatment of Acute Mania

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Educational Objectives:

The participant should be able to contrast the cost-effectiveness of aripiprazole, ziprasidone, risperidone, quetiapine, and olanzapine, in the acute treatment of mania in patients with bipolar I disorder.

Summary:

Objective: To estimate the cost-effectiveness of atypical antipsychotics (AAPs) in the treatment of acute mania in patients with bipolar I disorder from a managed care perspective.

Methods: The model estimated the cost-effectiveness (CE) ratios for each AAP when used as monotherapy for the acute (3-week) treatment of patients with bipolar mania. CE ratios were defined as the total annual cost per responder, and responders were defined as patients with a ≥50% improvement on the YMRS scale at 3 weeks. Data sources included published literature, package inserts, and primary data analysis of a managed care claims database. The median response rate for each AAP was used in the base case scenario; 45.5%, 50.0%, 58.0%, 53.3%, and 56.7% for aripiprazole, ziprasidone, risperidone, quetiapine, and olanzapine, respectively. Given the lack of head to head comparison studies involving all AAPs, response rates were obtained from individual studies for each AAP. Total annual costs were calculated based on 1.3 acute manic episodes per year and included costs of AAPs, concurrent medications, adverse events, and medical resource utilization. All costs were inflated to 2005 values. Incremental cost-effectiveness ratios were also calculated and sensitivity analyses were conducted.

Results: The total annual costs per patient were $7,897, $7,778, $7,807, $7,730, and $7,829 for aripiprazole, ziprasidone, risperidone, quetiapine, and olanzapine, respectively. Given the response rates and costs per patient listed above, the CE ratios were $17,356, $15,555, $13,460, $14,504, and $13,807, respectively.

Conclusion: These findings suggest that, among AAPs, treatment with risperidone may be the most cost-effective choice for acute management of mania in patients with bipolar I disorder. The results of this model are limited to the 3-week acute treatment of mania, thus no conclusions can be drawn about the cost-effectiveness of AAPs when used as maintenance therapy.

References:

1. Bryant-Comstock L, Stender M, Devercelli G. Health care utilization and costs among privately insured patients with bipolar I disorder. Bipolar Disorders. 2002:4:398-405.
2. Goldberg J, Harrow M, Grossman L. Course and outcome in bipolar affective disorder: a longitudinal follow-up study. Am J Psychiatry.1995;152:379-384.

NR960 Thursday, May 25, 12:00 PM - 2:00 PM

Stigmatizing Experiences in Patients With Mood and Anxiety Disorders

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to:

1. Understand the issues with stigma and discrimination because of Mood & Anxiety Disorders,
2. Have some knowledge about the Inventory of Stigmatizing Experiences,
3. Be aware of the need for further research and work towards defeating stigma.

Summary:

Background: Mood and Anxiety Disorders are very common and disabling psychiatric conditions. They usually run a chronic course with their symptoms waxing and waning. Although they do not impair functioning to such a severe extent as for example, Schizophrenia, they are still association with significant burden of disease[1]. Patients with Mood & Anxiety Disorders experience a significant amount of stigmatizing and discrimination because of their mental illness.

Method: We have developed an Inventory of Stigmatizing Experiences[2]. It is a questionnaire, which includes both a frequency and an intensity scale, and measures the prevalence and frequency of stigma experiences, with the underlying assumption being that the total score reflects the pervasiveness of stigma experienced across different life domains.

Results: Over 60 patients attending a specialized tertiary service looking after patients with Mood & Anxiety Disorders were screened with the Inventory of Stigmatizing Experiences. The results show that the experience of stigmatizing events and dis-

crimination because of mental illness is very high and occurs almost universally. Some further analysis based on age, gender and diagnosis is given. The need for further study in this population is emphasized.

Conclusion: Stigmatizing experiences and discrimination is common in patients with Mood & Anxiety Disorders, and requires further studying and work towards reducing it.

References:

1. Murray CL, Lopez AD. Alternative projections of mortality and disability by cause 1990-2020: Global burden of disease study. Lancet 1997; 349: 1498-1504.
2. Stuart H, Milev R, Koller M. The Inventory of Stigmatizing Experience: its development and reliability. World Psychiatry 2005; 4:S1.

NR961 Thursday, May 25, 12:00 PM - 2:00 PM

An Evaluation of Excessive Daytime Sleepiness in People With Epilepsy and Comorbid Depressive Symptoms Treated With Lamotrigine

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand the incidence of comorbid depression in people with epilepsy and the effects of antiepileptic drugs on daytime sleepiness.

Summary:

Objective:

Antiepileptic drugs (AEDs) are used for a variety of indications. Excessive daytime sleepiness (EDS) is a common side effect of many AEDs and is prevalent in people with epilepsy (PWE). Likewise, comorbid depression is often present in PWE and may also disrupt sleep patterns. The Epworth Sleepiness Scale (ESS) is a validated questionnaire which measures the likelihood of becoming drowsy during daytime activities. Scores > 10 suggest the presence of EDS. LTG has low reported rates of somnolence compared with other AEDs. This analysis evaluated the effects of LTG on EDS in a subset of PWE and comorbid depressive symptoms from a larger study.

Methods:

In this multicenter open-label study, LTG was added onto a stable AED regimen in the adjunctive phase and became a single agent in the monotherapy phase. Patients were eligible if they had epilepsy, exhibited at least minimal depressive symptoms but excluded if they had a MDD. ESS was completed at baseline, at the end of adjunctive (Week 19) and monotherapy (Week 36). Statistical analysis was done using paired t-tests.

Results:

Of the 158 PWE enrolled, 49 patients received phenytoin (PHT) and 30 patients received carbamazepine (CBZ) as the background AED. Mean baseline, end of adjunctive and monotherapy scores for the ESS in the PHT and CBZ subgroups respectively, were 10.2, 9.6, 9.0 and 9.3, 7.6, 5.8. Scores in the overall group were 9.7, 8.5 and 8.2. Change scores were significant at $p < 0.05$ for monotherapy.

Conclusion:

This evaluation suggests that some PWE and comorbid depressive symptoms experience EDS. The soporific effects of depression and AEDs did not worsen upon addition of LTG and improved during monotherapy. These data further confirm the variable effects of AEDs on sleep and wakefulness and suggest a relatively positive sleep-wake profile for LTG.

References:

1. Jones JE, Hermann BP, Barry JJ et al. Clinical assessment of Axis I psychiatric morbidity in chronic epilepsy: A multicenter investigation. J Neuropsychiatry Clin Neurosci 2005;17:172-179.
2. Foldvary-Schaefer N. Sleep complaints and epilepsy: The role of seizures, antiepileptic drugs and sleep disorders. J Clin Neurophysiology 2002;19(6):514-521.

NR962 Thursday, May 25, 12:00 PM - 2:00 PM

Efficacy of Aripiprazole in Highly Agitated Patients With Psychosis of Alzheimer's Disease

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to appreciate that Alzheimer's disease patients with associated symptoms of psychosis can also have a wide range of agitation levels. They should also be aware that aripiprazole effectively improves symptoms in patients with high agitation levels, as demonstrated by a pooled analysis of efficacy data from two 10-week placebo-controlled trials of institutionalized patients with Alzheimer's disease and associated psychosis.

Summary:

Objective: Assess the impact of baseline agitation on the efficacy of aripiprazole in reducing the behavioral symptoms and psychosis of Alzheimer's disease.

Methods: Institutionalized patients (N = 723; 55-95 y) with psychosis of Alzheimer's disease were randomized to receive aripiprazole 2-10 mg/d (n = 485) or placebo (n = 238) in two 10-week, double-blind, pivotal trials (004 and 005). Post-hoc analyses were performed on the efficacy data after stratifying patients by baseline agitation into high (n = 503) or low (n = 220) agitation groups. High agitation was defined as scores ≥4 and low agitation was defined as scores <4 on the Neuropsychiatric Inventory-Agitation/Aggression (NPI-A) item. Mean changes over time in clinical and behavioral status were assessed on the Clinical Global Impression-Improvement (CGI-I), and Cohen-Mansfield Agitation Inventory (CMAI) scales, and the NPI-Psychosis (NPI-P) and NPI-A items.

Results: In highly agitated patients, aripiprazole was associated with significantly improved CGI-I scores (at Weeks 2, 4, 8, and 10), CMAI scores (at all time points), and NPI-A scores (from Week 4 to endpoint), compared with placebo ($P < 0.05$). No significant differences in these measures were observed in patients with low agitation. Aripiprazole did not significantly improve NPI-P scores in patients experiencing high or low agitation. The most common aripiprazole-associated adverse events in trial 004 (≥5% incidence and twice that of placebo) were light headedness, abnormal gait, increased salivation, urinary incontinence, asthenia, and somnolence. The most common aripiprazole-associated adverse events in trial 005 were somnolence, back pain, urinary incontinence, abnormal gait, and infection.

Conclusions: Aripiprazole was associated with significant clinical improvement and significantly reduced symptoms of agitation in highly agitated patients with Alzheimer's disease, compared with placebo.

References:

1. Cummings JL, Tractenberg RE, Gamst A, et al: Regression to the mean: implications for clinical trials of psychotropic agents in dementia. Curr Alzheimer Res 2004; 1:323-328.

2. De Deyn P, Jeste DV, Swanink R, et al: Aripiprazole for the treatment of psychosis in patients with Alzheimer's disease: a randomized, placebo-controlled study. J Clin Psychopharmacol 2005; 25:463-467.

NR963 Thursday, May 25, 12:00 PM - 2:00 PM

Improving Understanding of the Research Consent in Mild Alzheimer's Disease and Mild Cognitive Impairment

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand the limitations of the methods to improve the understanding of the informed consent information among persons with Alzheimer's disease and mild cognitive impairment.

Summary:

Objective: Ethical research requires voluntary consent from a fully informed volunteer with decision-making capacity. Mild Cognitive Impairment (MCI) and mild Alzheimer's disease (AD) may impair patients' ability to give informed consent. We explored whether MCI and AD patients' level of understanding could be improved with an enhanced consent procedure in a small pilot study. *Methods:* Participants were 18 outpatients with AD and 11 with MCI (MMSE total score >=19). They were given information about a hypothetical clinical trial and randomized to receive information via Routine Consent Process (RCP) or Deficit Compensation Consent Process (DCCP). The DCCP used a graphically, voice-enhanced PowerPoint presentation to teach key components and target deficits in acquiring information. The MacCAT-CR Understanding subscale measured comprehension following presentation of RCP or DCCP (Trial 1) and after review (Trial 2). This data was analyzed with a repeated measures ANCOVA, controlling for total RBANS - a measure of global cognition. We recorded time to complete the consent process, demographics, and medical and neuropsychological information. *Results:* Time to complete DCCP was faster than RCP for both AD (24.1 versus 34.5; p=0.020) and MCI (19.6 versus 35.0; p<0.0001) groups. For AD outpatients at Trial 1, the mean MacCAT-CR Understanding subscale score was 12.0 for both the DCCP and RCP groups; whereas at Trial 2, the DCCP mean was 2.2 points higher than the RCP mean. MCI outpatients consented with DCCP understood, on average, 4.0 and 1.5 points more than those with RCP at Trials 1 and 2, respectively. *Conclusions:* On average, participants consenting with DCCP consistently understood the same amount or more in less time than those using RCP. Though small sample sizes limited statistical power, results suggest that enhanced procedures, such as DCCP, may improve participant understanding of consent information. Further studies with larger sample sizes appear warranted.

References:

1. Appelbaum PS. Involving decisionally impaired subjects in research: The need for legislation. American Journal of Geriatric Psychiatry 10(2):120 -4, 2002; 10(2):120-124.

2. Dunn LB, Jeste DV. Enhancing informed consent for research and treatment. Neuropsychopharmacology 2001; 24(6):595-607.

NR964 Thursday, May 25, 12:00 PM - 2:00 PM

Prevalence of Bipolar Disorder Risk Among Anti-Depressant Nonresponders

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Educational Objectives:

To better understand the risk of undetected bipolar disorder in patients treated for unipolar depression.

Summary:

Objective: The objective of this study was to assess the rate of bipolar disorder (BPD) among unipolar depression patients currently in treatment.

Method: Psychiatrists from community and private practice clinic settings randomly selected patients with unipolar depression who had one or more prior antidepressant (AD) medication failures. Patients with a diagnosis of BPD, OCD, or schizophrenia were excluded. Medical record abstraction obtained patient history as well as current and prior AD medication use. A self-administered patient survey collected demographics, current bipolar symptoms via the Mood Disorder Questionnaire (MDQ), and comorbid health problems for self.

Results: Data were collected from 602 patients. A total of 18.6% of patients screened positive on the MDQ and this rate was not impacted by the number of prior AD failures or patient demographics. There were 74 patients (12.3%) who reported a prior history of BPD of which the psychiatrist was not aware. The positive MDQ rate in this subgroup was 41.9%.

Conclusions: These data suggest that clinicians should carefully screen for BPD among their unipolar patients, regardless of AD treatment history or demographic sub-group. Further consideration should be given to identifying and evaluating those with prior BPD history.

Research supported by GlaxoSmithKline.

References:

1. Hirschfeld RMA et al: Screening for bipolar disorder in patients treated for depression in a family medicine clinic. JABFP 2005;18: 233-239.

2. Das AK et al: Screening for bipolar disorder in a primary care practice. JAMA 2005;293: 956-963.

NR965 Thursday, May 25, 12:00 PM - 2:00 PM

Cognitive Characteristics in Somatizers With Anxiety Symptoms

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Educational Objectives:

Assuming that somatization closely interacts with anxiety symptom, one might speculate that anxiety symptom will produce the significant differences in development, course and treatment of somatization: and the cause of these differences will be elucidated on the cognitive aspect.

Under the background described above, this study attempted to examine the cognitive characterisctics in terms of the somatosensory amplification and the symptom interpretation in patients with somatization accompanying anxiety symptom in comparison with those accompanying no anxiety symptom.

Summary:

Objective:

Assuming that somatization closely interacts with anxiety symptom, one might speculate that anxiety symptom will produce the significant differences in development, course and treatment of somatization: and the cause of these differences will be elucidated on the cognitive aspect.

Under the background described above, this study attempted to examine the cognitive characterisctics in terms of the somatosensory amplification and the symptom interpretation in patients with somatization accompanying anxiety symptom in comparison with those accompanying no anxiety symptom.

Methods:

To fulfill the above objective, this study used the following tools in patients exhibiting the somatic symptoms of unknown organic etiology: (1) Minnessota Multiphasic Personality Inventory - Korean Version (MMPI-K), (2) Symptom Checklist-90-Revision (SCL-90-R), (3) Somato-sensory Amplification Scale (SSAS) (4) Symptom Interpretation Questionnaire(SIQ).

Based in 12 questions as the somatization scale of SCL-90-R, patients' somatization was screened under the standard of T score of 60. Moreover, Patients were divided into anxiety group (n=163) and non-anxiety group (n=135) under the standard of scale 7, T score of 60.

Results:

The amplification of sensation was greater in anxiety group than non-anxiety group. In regard to the symptom interpretation, anxiety group showed higher levels of physical interpretation, psychological interpretation and catastrophic interpretations than non-anxiety group. Besides, multiple regression analysis showed the following:

(1) Somatization was affected by somatosensory amplification, physical interpretation. psychological interpretation in corresponding order in anxiety group; (2) Somatization was affected by physical interpretation and the somatosensory amplification in corresponding order in non-anxiety group; and (3) Somatization was not affected by psychological, catastrophic and environmental interpretations in non-anxiety group with statistical significance.

Conclusion:

At the conclusion of this presentation, the participant should be able to recognize on the cognitive aspect, the somatosensory amplification and the symptom interpretation were more severely distorted in patients accompanying anxiety symptom than those accompanying no anxiety symptom.

References:

1. Sadock BJ, Sadock VA:Kaplan and Sadock's Comprehensive Textbook of Psychiatry 7th edition: The somatization disorder. Philadelphia, Lippincott Williams & Wilkins, 2000.
2. Sadock Bj, Sadock Va: Synopsis of psychiatry, 9th edition:Somatoform disorder. Philadelphia, 2002.

NR966 Thursday, May 25, 12:00 PM - 2:00 PM

The Hostility Subscale of the SCL90 Helps Identify Bipolar Outpatients

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Educational Objectives:

At the conclusion of this presentation, the participants should become familiar with the SCL90, and should be able to recognize bipolar patients from their SCL90 hostility subscale scores

Summary:

Introduction: Hostility and irritability are commonly seen symptoms in bipolar patients especially those with the type II or spectrum disorder. The SCL90 has a subscale of hostility that may be useful in increasing the suspicion index of bipolar diagnosis in patients presenting to a psychiatrist for a first visit

Methods: A chart review was performed on all patients currently being seen in a private, rural, outpatient psychiatric clinic. Data collected included patient demographics and SCL-90 scores completed prior to the first office visit. All patients were then given a diagnosis by their treating psychiatrist aided by the MiniSCID.

Results: 903 patients (70% of the current clinic population) had completed the SCL-90 at the start of their treatment. Their average age is 43.8(±13.8) years old. 34% of patients have a current clinical diagnosis of bipolar disorder (19% are BPI and 15% are BPII). Nonbipolar patients had an average hostility score on the SCL-90 of 0.99(±0.85). Bipolar patients had a significantly higher average score of 1.38(±1.0) ($p<0.001$). There was no difference between BPI and BP II patients (1.37 and 1.39 respectively). 70% of patients who had a score of 3.5 or higher had a diagnosis of a bipolar disorder. Only 26% of patients with a hostility score below 1 had a diagnosis of a bipolar disorder.

Conclusions: The hostility subscale of the SCL90 is easy to use and a useful additional tool in identifying bipolar patients at their first office visit.

References:

1. Benazzi F, Akiskal H: Irritable-hostile depression: further validation as a bipolar depressive mixed state. J Affect Disord 2005; 84:197-207.
2. Hunter EE, Penick EC, Powell BJ, Othmer E, Nickel EJ, Desouza C: Development of scales to screen for eight common psychiatric disorders. J Nerv Ment Dis 2005; 193:131-5.

NR967 Thursday, May 25, 12:00 PM - 2:00 PM

Childhood Predictors for Cigarette Smoking Among Males: A Prospective Birth-Cohort Study

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to identify childhood psychopathology, especially ADHD and conduct symptoms, and childhood depressiveness, as a risk factor for smoking in later life.

Summary:

Objective: To study childhood psychopathological deviance as a precursor for cigarette smoking among late-adolescent males in a representative birth-cohort study.

Design: In 1989, a general population sample of 2946 8-year-old boys was collected. Three different informant sources were used: parents, teachers, and the boys themselves. The follow-up was ten years later in 1999, when the boys were called up for their obligatory military service at age 18. Information about cigarette smoking frequency was obtained from 78.3% (n= 2307) of the original sample.

Setting: Finland, nation-wide. In 1989 at schools, in 1999 at the mandatory military call-up.

Participants: General population sample of Finnish boys born in 1981.

Measurements: At age eight, the Rutter A2 scale, Rutter B2 scale and Child Depression Inventory (CDI) were used. At age 18, self-reported cigarette smoking during the preceding six months was determined.

Results: At age 8, hyperactive and conduct problems, child's self-reported depressive symptoms and family background predicted smoking in late adolescence. In the multivariate analysis

including information from all three different informants, only family background and reports provided by children and teachers predicted subsequent heavy smoking.Teacher-reported emotional problems were associated with lower occurrence of heavy smoking.

Conclusions: In addition to childhood ADHD and conduct symptoms, childhood depressiveness may increase the risk of adult smoking whereas childhood anxiety may protect boys for adult smoking. The school health care system has a potential role to recognize those children at risk for daily smoking.

References:

1. Fergusson DM, Horwood LJ, Ridder EM. Show me the child at seven: the consequences of conduct problems in childhood for psychosocial functioning in adulthood. J Child Psychol Psychiatry 2005;46:837-849.
2. Sacco KA, Bannon KL, George TP. Nicotinic receptor mechanisms and cognition in normal states and neuropsychiatric disorders. Review. J Psychopharmacol 2004;18:457-74.

NR968 Thursday, May 25, 12:00 PM - 2:00 PM

Does Schizophrenic Patients With an Abnormal PE Distribution in Their Erythrocyte Membranes Differ From Schizophrenic Patient Without This Abnormality in Clinical Phenomenology and in Treatment Response?

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Educational Objectives:

We wanted to compare clinical features and treatment response between schizophrenic patients with erythrocyte membrane lipid abnormality (G1) versus schizophrenic patients without this abnormality (G2)

Summary:

Background We have previously shown the existence of a significant decrease in the asymmetrical PE gradient in Extended Release ythrocyte membranes in the 2/3 (G1) of a group of schizophrenic patients (N=68). The PE ratio of the remaining 1/3 schizophrenic patients (G2) was identical to the one of a group of healthy controls (G0). The PE mean ratio in the G1 group (8/92) was significantly higher ($p< 0.05$) compared to the PE mean ratio in the G0 and G2 groups. The nature of the antipsychotic treatment in the G1 and G2 groups was not correlated with the modification of the asymmetrical PE gradient in RBC membranes.

Method All schizophrenic patients (N=68) from our study were evaluated for their psychopathology (PANSS, CGI, GAF), medical treatment, age of onset, number of hospitalisations, family history of psychosis, treatment response. A multivariate statistical analysis was applied in order to identify significant difference between G1 and G2 on these criteria.

Results G1 and G2 group didn't differ by age, gender, and medication (antipsychotic and other psychotropic drug). Significant differences were seen in positive and disorganization of subscores of the PANSS, CGI total scores, and specific GAF items scores.

References:

1. Ponizovsky AM, Modai I, Nechamkin Y, Barshtein G, Ritsner MS, Yedgar S, Lecht S, Bergelson LD. Phospholipid patterns of erythrocytes in schizophrenia: relationships to symptomatology Schizophr Res. 2001 Oct 1;52(1-2):121-6.
2. Glen AI, Glen EM, Horrobin DF, Vaddadi KS, Spellman M, Morse-Fisher N, Ellis K, Skinner FS. A red cell membrane abnormality in a subgroup of schizophrenic patients: evidence for two diseases. Schizophr Res. 1994 Apr;12(1):53-61.

NR969 Thursday, May 25, 12:00 PM - 2:00 PM

Meta-Analysis of Neuropsychiatric Inventory Domains in Three, Six-Month Trials of Memantine in Moderate to Severe Attention Deficit

Jason T. Olin, Ph.D. *Forest Research Institute, Harborside Financial Center, Plaza V, 19th Floor, Jersey City, NJ, 07311*, Jeffrey L. Cummings, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to assess the efficacy of memantine on behavioral disturbances in patients with moderate to severe Alzheimer's disease.

Summary:

Objective: Memantine, a moderate affinity, uncompetitive N-methyl-D-aspartate (NMDA) receptor antagonist, is approved in the U.S. and in Europe for the treatment of moderate to severe Alzheimer's disease (AD). To assess the effects of memantine on behavioral disturbances in AD, a meta-analysis of three large-scale, randomized, placebo-controlled clinical trials was performed.

Methods: NPI total scores and individual domains from three, 6-month memantine trials in moderate to severe AD patients were analyzed (MEM-MD-01, van Dyck et al, in preparation; MEM-MD-02, Tariot et al., 2004; MRZ 90001-9605, Reisberg et al., 2003). All trials were randomized, double-blind, parallel-group designs comparing memantine (10 mg b.i.d.) to placebo. MEM-MD-02 allowed concomitant donepezil therapy (6 months, stable for ≥3 months). Standardized mean differences (SMD) were calculated using fixed-effect models; random effects models were used when evidence of heterogeneity was observed (Chi^2 $P \leq .10$). Analyses were based on Intention-to-Treat populations using a last observation carried approach for replacement of missing values.

Results: Change from baseline on NPI total score at study endpoint for each trial revealed a statistically significant advantage of memantine over placebo in the MEM-MD-02 study only (P= .002). When data from all three trials were combined and analyzed, the NPI total score showed a homogeneous effect size in favor of memantine treatment (Chi^2=3.32, P=.19; SMD= -0.17 [95%CI -0.30, -0.04], P=.01). Additionally, several NPI domains demonstrated statistically significant treatment differences in favor of memantine and all were homogeneous: delusions (Chi^2=2.33, P= .31; SMD= -0.14 [95%CI -0.27, -0.02], P=.03), agitation/aggression (Chi^2=2.48, P=.29; SMD= -0.24 [95%CI -0.37, -0.11], P= .0003), and irritability/lability (Chi^2=3.49, P=.17; SMD= -0.13 [95%CI -0.26, 0.0], P=.05). Heterogeneity was seen on hallucinations and depression/dysphoria.

Conclusions: These findings suggest that memantine treatment of 6-months duration can provide a reduction in specific behavioral disturbances in patients with moderate to severe AD, including agitation/aggression, delusions, and irritability/lability.

References:

1. Reisberg B, Doody R, Stöffler A, et al. Memantine in moderate-to-severe Alzheimer's disease. N Engl J Med. 2003;348(14):1333-1341.
2. Tariot PN, Farlow MR, Grossberg GT, et al. Memantine treatment in patients with moderate to severe Alzheimer disease already receiving donepezil: a randomized controlled trial. JAMA. 2004;291(3):317-324.

NR970 Thursday, May 25, 12:00 PM - 2:00 PM

Study of Cortical Excitability and Inhibitory Mechanisms With TMS in Social Anxiety: Preliminary Results

Stefano Pallanti, Sr., M.D. *Inst. Neuroscienze, Viale Ugo Bassi 1, Firenze, 50137, Italy*, Ilenia Pampaloni, Jr., M.D., Massimo Cincotta, Alessandra Borgheresi, Fabio Giovannelli, Gaetano Zaccara

Educational Objectives:

At the end of this presentation participants should be able to understand the hypotisized machanisms in the genesis of Social Anxiety

Summary:

Background: Social Anxiety (SA) is the third psychiatric disorder (Kessler et al., 1994) with prevalence rates of 1.9-18.7%. Recently, neurofunctional imaging studies comparing subjects with SA with healthy controls, reported a consistent increases in the amygdala (Lorberbaum JP, 2004, Veit et al., 2002; Stein et al., 2002; Tillfors et al., 2001), changes in the lateral paralimbic regions and occipital cortices.

A current hypothesis underlying pathophysiology of social anxiety involves the dopaminergic system: SA Subjects show a reduction in D2 striatal binding (Schneier et al., 2000; Tihonen 1997); Parkinson patients with comorbid SA show a reduction in HVA levels (Johnson 1994), and there are evidences about the efficacy of dopaminergic drugs in SA. Furthermore, SA is common among Parkinson patients (Stein et al., 1995).

We hypothesized that subjects with SA disorder may have an altered cortical excitability, given previous imaging results showing changes in cortical activity and that SA patients show at Transcranial Magnetic Stimulation (TMS) a pattern Parkinson-like.

Method: We recruited n=5 SA subjects and n=11 Healthy Controls. We have utilized TMS on Primary Motor Cortex (M1) in order to study neuronal excitability and cortical inhibitory mechanisms. These has been achieved by examining EMG recording Motor Evoked Potentials (MEP). We measured MEP, Motor threshold, Cortical Silent Period (CSP), paired pulse inhibition both in patients and healthy controls.

Preliminary Results: CSP is reduced (p=.055) in SA subjects. CSP represent an index of cortical inhibition.

Discussion: SA subjects show a reduction of CSP, that is a reduction of inhibition, and therefore an increased cortical excitability. Also in Parkinson CSP is reduced. This result go with data of Literature showing a strong relationship between SA and Parkinson Disease: these condition are often comorbid and subject with Anxiety Disorders (and particular SA) are more likely to develop Parkinson Disease.

References:

1. Lorberbaum JP, Kose S, Johnson MR, Arana GW, Sullivan LK, Hamner MB, Ballenger JC, Lydiard RB, Brodrick PS, Bohning DE, George MS.Neural correlates of speech anticipatory anxiety in generalized social phobia. Neuroreport. 2004 Dec 22;15(18):2701-5.

2. Schneier FR, Liebowitz MR, Abi-Dargham A, Zea-Ponce Y, Lin SH, Laruelle M.Low dopamine D(2) receptor binding potential in social phobia.

NR971 Thursday, May 25, 12:00 PM - 2:00 PM

A Randomized, Double-Blind, Placebo-Controlled Trial of Sodium Oxybate in Fibromyalgia Syndrome

Ashwin A. Patkar, M.D. *Duke University, Psychiatry, 4323 Ben Franklin Boulevard, suite 700, Durham, NC, 27704*, Robert M. Bennett, M.D., Joel E. Michalek, Ph.D., Harry Cook, R.Ph., Philip D. Perera, M.D., Prakash S. Masand, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant will be able to understand the clinical features and therapeutic options including the potential benefit of sodium oxybate in the treatment of fibromyalgia syndrome.

Summary:

Objectives: There is no FDA-approved medication for treating fibromyalgia syndrome [FMS]. Sodium oxybate (Xyrem®) is currently approved for the treatment of cataplexy and excessive daytime sleepiness in patients with narcolepsy. We conducted a proof-of-principle study to examine the efficacy and safety of Oxybate in FMS. **Methods:** 195 patients with primary FMS were randomized to receive oxybate (4.5 g or 6 g per day) or placebo for 8 weeks. The primary outcome variable [POV] was a composite of changes from baseline in three co-primary, self-report measures: Pain Visual Analog Scale [PVAS], Fibromyalgia Impact Questionnaire [FIQ]; and Patient Global Assessment [PGA]. Secondary outcome measures included changes in sleep quality [SLP], and the Total Tender Point Count, [TTP]. Intent-to-treat [ITT] analyses to examine changes from baseline and a post-hoc correlation analysis between the PVAS and SLP were performed.**Results:** The ITT population included 188 patients [placebo, n=64; oxybate 4.5g, n=58; oxybate 6g, n=66], of whom 147 [78%] completed the trial. Significant benefit in the POV was seen with both doses of oxybate compared with placebo [4.5g, p=0.005]. SLP was improved with both dosages of oxybate [4.5g, p=0.004]. The TTP was significantly improved only with the 6g dose [p = 0.05]. A significant correlation was seen between change in PVAS and change in SLP [r=0.55, p<0.001]. Oxybate was well tolerated, as illustrated by the high rate of study completion. As expected, dose-related nausea and dizziness were observed more with oxybate but there were no unexpected adverse events.**Conclusion:** Oxybate therapy of FMS was safe and significantly improved the major symptoms of FMS [pain, tenderness, insomnia]. Improved sleep quality appears to contribute to the reduction in pain. Sodium oxybate (Xyrem®) represents a novel therapeutic option for FMS and warrants further study.

References:

1. Scharf MB, Baumann M, Berkowitz DV: The effects of sodium oxybate on clinical symptoms and sleep patterns in patients with fibromyalgia. J Rheumatol 2003; 30:1070-1074.

2. Mamelak M, Black J, Montplaisir J, Ristanovic R: A pilot study on the effects of sodium oxybate on sleep architecture and daytime alertness in narcolepsy. Sleep. 2004 ; 27(7):1327-34..

NR972 Thursday, May 25, 12:00 PM - 2:00 PM

Can the Disabling Aspects of Depression in Dementia Be Ameliorated With Resistance Exercise?

Janis B. Petzel, M.D. *MaineGeneral Health, Geriatric Psychiatry, 37 Winthrop Street, Hallowell, ME, 04347*, Vince S. Thomas, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the impact of resistance exercise on depression and function in dementia

Summary:

Background: Studies have shown an almost dose-response relationship between depressive symptoms and disability in the elderly. Resistance exercise has a positive impact on various aspects of mood and function in the elderly, although few studies have been accomplished with demented subjects. This study ex-

amines the effects of depression in relationship to overall function in the context of a randomized, controlled resistance exercise intervention in persons with dementia.

Methods: Subjects previously diagnosed with dementia were recruited from an Alzheimer's Boarding Home in rural New England and randomized into either a 16-week resistance exercise intervention (N=12) or provided with care-as-usual (N=12). The resistance exercise intervention was performed by trained boarding home staff using Therabands three times a week for approximately 1 hour. Overall function was assessed using the Clinical Dementia Rating Scale (CDR) sum-of-boxes method. Depression was assessed using the Dementia Mood Assessment Scale (DMAS).

Results: Higher DMAS scores indicate worsening depression. Likewise, higher CDR scores indicate increased functional impairment. When the change in CDR score is plotted against change in DMAS scores, 7/12 people in the care-as-usual group had increases in both CDR and DMAS, with 9/12 with increased DMAS and 10/12 with increased CDR. In the exercise intervention group, 3/12 worsened in both mood and function, 6/12 had higher DMAS scores and 7/12 had higher CDR scores but 2/12 improved in both DMAS and CDR (compared to 0/12 in the care-as-usual group).

Conclusions: Depression symptoms and functional impairment continued to accumulate over time in both the exercise and the care-as-usual group in this demented population. Worsening depression was strongly related to functional decline in the care-as-usual group. However, the exercise group declined less dramatically, and in many cases, improved in either mood, overall function or in both.

References:

1. Beekman AT, Deeg DJ, Braam AW, et al: Consequences of major and minor depression in later life: a study of disability, well-being and service utilization. Psychol Med 1997; 27:1397-1409.
2. Lebowitz BD, Pearson JL, Schneider LS, et al: Diagnosis and treatment of depression in late life: consensus statement update. JAMA 1997; 278:1186-1190.

NR973 Thursday, May 25, 12:00 PM - 2:00 PM

A Prospective Longitudinal Study of the Course of BDD

Katharine A. Phillips, M.D. *Butler Hospital/Brown University, 345 Blackstone Boulevard, Providence, RI, 02906*, Maria E. Pagano, Ph.D., William Menard, B.A., Robert L. Stout, Ph.D.

Educational Objectives:

The educational objective of this poster is to become familiar with the course of body dysmorphic disorder (remission and relapse) in the first prospective study of the course of this relatively common disorder.

Summary:

Objective: Prospective studies of the course of BDD, a relatively common and severe disorder, have not previously been conducted. This prospective naturalistic observational study investigated remission and relapse in individuals with BDD over one year of follow-up. Method: The Longitudinal Interval Follow-Up Evaluation (LIFE) obtained data on weekly BDD symptom status and treatment received over one year for 183 broadly ascertained subjects. Probabilities of full remission, partial remission, and relapse during this year were examined. Full remission was defined as minimal or no BDD symptoms -- and partial remission as less than full DSM-IV criteria -- for at least eight consecutive weeks. Relapse was defined as meeting full BDD criteria for at least two consecutive weeks after attaining partial or full remission from BDD. Results: Over 1 year, the probability of full remission from BDD was only .09, and the probability of partial remission was .21. Even though 84.2% of subjects received mental health treatment during the 1-year period, mean BDD severity scores during this year reflected full DSM-IV criteria for BDD, and the mean proportion of time that subjects met full BDD criteria was 80%. Gender and ethnicity did not significantly predict remission from BDD. Among those subjects who partially or fully remitted from BDD, the probability of relapse was .15. Conclusions: These findings indicate that BDD tends to be chronic. Remission probabilities were lower than reported for mood disorders, most anxiety disorders, and personality disorders in studies using very similar methodology to ours.

References:

1. Phillips KA, Pagano ME, Menard W, Stout RL: A prospective follow-up study of the course of body dysmorphic disorder. Am J Psychiatry, in press.
2. Phillips KA, Menard W, Fay C, Weisberg R: Demographic characteristics, phenomenology, comorbidity, and family history in 200 individuals with body dysmorphic disorder. Psychosom 2005; 46:317-332.

NR974 Thursday, May 25, 12:00 PM - 2:00 PM

A Double-Blind Comparison of Citalopram and Risperidone for the Treatment of Dementia-Related Behavioral and Psychotic Symptoms

Bruce G. Pollock, M.D. *Western Psychiatric Institute & Clinic, Psychiatry, 3811 O'Hara Street, Pittsburgh, PA, 15213-2593*, Benoit H. Mulsant, M.D., Jules Rosen, M.D., Sati Mazumdar, Ph.D., Richard Blakesley-Ball, B.S., Patricia R. Houck, M.S., Kimberly A. Huber, M.P.H.

Educational Objectives:

To present new information from a recently completed controlled clinical trial comparing a second generation atypical antipsychotic and SSRI for the treatment of non-cognitive behavioral symptoms.

To discuss the limitations of current pharmacotherapy for psychosis and agitation.

To highlight controversies in our current diagnostic nosology of psychosis in dementia and its neurochemical basis.

Summary:

Introduction: Previously, we found that the highly selective 5HT reuptake inhibitor (SSRI), citalopram, is acutely beneficial for both psychotic and non-psychotic symptoms in non-depressed, elderly patients hospitalized for up to 17 days for non-cognitive behavioral symptoms (NCBS). We have recently completed a 12-week controlled study comparing the acute and long-term efficacy of citalopram and risperidone for the treatment of NCBS. **Methods:** 103 patients with dementia who were hospitalized with at least one moderate to severe target behavioral or psychotic symptom (aggression, agitation, hostility, suspiciousness, hallucinations, or delusions) were randomly assigned to receive either citalopram or risperidone under double-blind conditions for up to 12 weeks. Patients with depressive symptoms (Cornell >12) were excluded from participation. Inpatients were discharged to a nursing home, personal care home, or residential home for continued treatment once they improved sufficiently. All subjects were assessed with the Neurobehavioral Rating Scale (NBRS) and with the UKU Side Effect Rating Scale at baseline and at weekly/bi-weekly intervals. **Results:** The overall completion rate was 44% with completion rates of 47% and 40% for citalopram and risperidone, respectively (these rates are not significantly different; p= 0.46). Neither treatment group showed a significant pre-post-treatment change in agitation symptoms; while significant pre-post-treatment decreases in psychosis symptoms were noted in both

groups. Pre-post-treatment changes for both NBRS-agitation and NBRS-psychosis symptoms did not differ significantly between the two groups. Significant increases in rigidity and EPS were seen in both treatment groups; the risperidone treatment group also showed a significant increase in UKU-total score. Overall, changes in UKU-total score differed significantly between the groups (p=0.013). **Conclusions:** Citalopram and risperidone were similarly efficacious in the treatment of behavioral and psychotic symptoms in patients with dementia. Patients treated with risperidone experienced a significantly higher burden of side effects. Sources of Support: R01 MH59666, K24 MH065416, RR-00056

References:

1. Pollock BG, Mulsant BH, Rosen, J, Sweet RA, Mazumdar S, et al.: Comparison of citalopram, perphenazine and placebo for the acute treatment of psychosis and behavioral disturbances in hospitalized, demented patients. Am J Psychiatry 2002; 159:460-465.
2. Sweet RA, Pollock BG, Sukonick DL, Mulsant BH, Rosen, J, Klunk WE, et al.: The 5HTTLPR-polymorphism confers libility to a combined phenotype of psychotic and aggressive behavior in Alzheimer's disease. International Psychogeriatrics 2001; 13:401-409.

NR975 Thursday, May 25, 12:00 PM - 2:00 PM

Healthcare Resource Utilization and Cost of Bipolar I Disorder With and Without Psychotic Symptoms

Sara Poston, Pharm.D. *Thomas Jefferson University, Health Policy, 1125 Trenton-Harbourton Road, Titusville, NJ, 08560,* Chris M. Kozma, Ph.D., Dennis M. Meletiche

Educational Objectives:

At the conclusion of this presentation, the participant should be able to describe and contrast the demographic characteristics of bipolar I patients with and without psychosis, as well as compare health resource utilization and costs between bipolar I patients with and without psychosis.

Summary:

Objective:
To compare the healthcare utilization and costs between patients with a diagnosis of bipolar I disorder with psychotic symptoms (BPP) to patients with bipolar I disorder without psychotic symptoms (BPO).
Methods:
We conducted a retrospective, independent group analysis using pharmacy and medical claims from a large national managed care database. Patients in each cohort were identified based on their first claim for a bipolar diagnosis during the 2003 calendar year. T-tests and chi-square tests were used to compare variables between the two groups.
Results:
Of the 8,221 patients who met study criteria, 7.9% of the BPP group (n=5,108) had at least one mental health-related hospitalization, compared to 4.0% of the BPO group (n=3,113, p<0.0001). Mean mental-health related hospital costs per patient in the BPP group were $625 (SD $3,326) compared to $283 (SD $2,223) in the BPO group (p<0.0001). Overall mean medication costs were $2,638 (SD $3,765) in the BPP group compared to $2,397 (SD$3,482, p=0.003), while mean costs for outpatient visits (other than physician visits) were not significantly different (p=0.078). Overall mean healthcare costs were $10,263 (SD $19,962) in the BPP group compared to $8,649 (SD $15,132) in the BPO group (p<0.0001).
Conclusions:
Patients with bipolar I disorder with psychotic symptoms had higher healthcare utilization and costs compared to patients without psychotic symptoms. Research on interventions targeting bipolar patients with psychotic symptoms may be warranted.

References:

1. Goldberg J, Harrow M, Grossman L: Course and outcome in bipolar affective disorder: a longitudinal follow-up study. Am J Psychiatry 1995; 152:379-384.
2. Akiskal H, Bourgeois M, Angst J, et al: Re-evaluating the prevalence of and diagnostic composition within the broad clinical spectrum of bipolar disorders. Journal of Affective Disorders 2000; 59: S5-S30.

NR976 Thursday, May 25, 12:00 PM - 2:00 PM

Sexual Orientation and Relationship Choice in Borderline Personality Disorder Over Ten Years of Prospective Follow-Up

D. Bradford Reich, M.D. *McLean Hospital, Psychiatry, 115 Mill Street, Belmont, MA, 02478,* Mary C. Zanarini, Ed.D., Frances R. Frankenburg, M.D.

Educational Objectives:

At the conclusion of this presentation, participants should have a greater understanding of differences in the prevalence of homosexual and bisexual orientation between patients with borderline personality disorder and patients with other personality disorders. In addition, participants should have a greater understanding of differences in the prevalence of same-sex intimate relationships between patients with borderline personality disorder and patients with other personality disorders.

Summary:

Objective: This study assessed the prevalence of homosexuality, bisexuality, and same-sex relationships in a sample of 362 hospitalized subjects, 290 with BPD and 72 comparison subjects with other personality disorders.
Method: At baseline and at 2-year follow-up periods, subjects diagnosed with BPD and comparison subjects with other personality disorders were asked in a structured interview to specify their sexual orientation and whether they had had an intimate relationship with a same-sex partner.
Results: Subjects with BPD were significantly more likely than comparison subjects to report homosexual or bisexual orientation at baseline or in one of the follow-up periods. In addition, they were more likely to report than comparison subjects to report having an intimate same-sex relationship. There were no signficant differences between male and female borderline patients in the prevalence of reported homosexual or bisexual orientation or in the prevalence of reported same-sex intimate relationships.
Conclusions: The results of this study underscore the need for clinicians to be aware that homosexual orientation, bisexual orientation, and having same-sex intimate partners may be more common in both male and female patients with BPD than in patients with other personality disorders.

References:

1. Zubenko GS, George AW, Soloff PH, et al: Sexual practice among patients with borderline personality disorder. Am J Psychiatry 1987; 144:748-752.
2. Dulit RA, Fyer MR, Miller FT, et. al: Gender differences in sexual preference and substance abuse of inpatients with borderline personality disorder. J Pers Dis 1993; 7: 182-185.

NR977 Thursday, May 25, 12:00 PM - 2:00 PM

The Effect of Personality Characteristics and Mental Health on Academic Achievement in Medical Students

Hyo Deog Rim, M.D. *Kyungpook National University Hospital, Psychiatry, 50, Samdeok-dong 2-ga, Jung-gu, Daegu, 700-721, Republic of Korea,* Su Ryong Kim, M.D., Sang Heon Kim, M.D., Seung Hee Won, M.D., Gyung Ah Cho, M.D.

Educational Objectives:

This presentation provides information about the need of considerations of the mental hygine and some aspect of personality characteristics for adequate education of medical students who have to deal with greater stressors in their school days. At the conclusion of this presentation the participant should be able to demonstrate the importance of emotional stability of the medical students and the importance of developing relevant programs for their mental health by the faculties in medical school.

Summary:

The effect of personality characteristics and mental health on academic achievement in medical students

Objectives: This study investigated personality characteristics and mental health in medical students before the beginning of the school year, related the results with final academic achievements, and obtained the basic data that are necessary for adequate education and life guidance of medical students.

Methods: The subjects comprise 430 medical students; 424 of whom successfully completed the 1st year course but the rest 6 students failed. Of those, 402 completed the MMPI, SCL-90-R, BDI, TAS-20K. We defined the medical students as the risk group who scored high scores of MMPI(>70 in at least 1 of 10 clinical measures), SCL-90-R(>70 in at least 1 of 9 clinical measures), BDI(>16), and TAS-20K(>61). We used the 1st year course scores to evaluate their academic achievement.

Results: Most of the students who failed the 1st year course belonged to the risk group than others. The risk group significantly showed lower scores on academic achievements. There were negative correlations between psychopathic deviance(M4), schizophrenia(M8), hypomania(M9) and academic grade. There were positive correlations between masculinity-feminity(M5) and academic grade. There were also negative correlations between BDI score and academic grade.

Conclusion: We predicted that male students who failed or scored lower academic achievement after 1 year's academic work would have had tendency to belong to the risk group at the time of the beginning of the semester. Through this study we found that they significantly belonged to the risk group and that some personality characteristics such as severe psychopathology, gender role flexibility and depression correlated much with low academic achievements. We concluded that some personality characteristics and mental health such as severe psychopathology, gender role flexibility, obsession-compulsion, social introversion, negative emotion, psychoticism, depression, interpersonal sensitivity, phobia significantly influenced on academic achievements.

References:

1. Journal Article - Bramness JG, Fixdal TC, Vaglum P: Effect of medical school stress on the mental health of medical students in early and late clinical curriculum. Acta Psychiatr Scand 1991; 84:340-345.

2. Journal Article - Lloyd C, Gartrell NK(1981): Sex differences in medical student mental health. Am J Psychiatry 1981; 138:1346-1351.

NR978 Thursday, May 25, 12:00 PM - 2:00 PM

Gender and Psychotropic Medication Use: The Role of Intimate Partner Violence

Sarah E. Romans, M.B. *University of Toronto, Centre for Research in Women's Health, 790 Bay Street, 7th Floor, Toronto, ON, M5G 1N8, Canada,* Marsha M. Cohen, M.D., Tonia Forte, M.S.C., Janice Du Mont, Ed.D., Ilene Hyman, Ph.D.

Educational Objectives:

At the end of this presentation, the participant should be able to discuss the cross sectional association between increased use of psychotropic medication over the previous one month by women and men who report experiencing physical or sexual intimate partner abuse in the preceding five year.

Summary:

Objective: Women use more psychotropic medications than men; we tested the hypothesis that women's increased medication use may be linked to greater exposure to intimate partner violence (IPV).

Method: Using data from the 1999 Canadian General Social Survey, the use of medications for sleep, depression and anxiety were assessed. Rates of medication use by women and men exposed to IPV (physical, sexual, emotional and financial) were compared to rates of those reporting no IPV.

Results: Women were more likely than men to report using medications for sleep (11.0% versus 7.0%, $p<0.0001$), anxiety (7.6% versus 4.6%, $p<0.001$) and depression (5.7% versus 3.2%, $p<0.001$). More women (14.9%) than men (9.6%) reported use of any of these medications ($p<0.0001$). Among women, medication use was significantly higher among those reporting emotional, financial, physical, and sexual IPV compared to those reporting no IPV. For men, medication use was higher among those reporting emotional IPV. The link between IPV and all types of medication use was present after adjusting for sociodemographic and health variables.

Conclusion: This study is the first to show that IPV may explain some of the increased psychotropic medication use by women. IPV should be included in studies investigating medication use.

References:

1. Mazza D, Dennerstein, L: Psychotropic drug use by women: could violence account for the gender difference? J Psychosom Obstet Gynaecol 1996; 17(4), 229-234.

2. Cooperstock R: Sex differences in psychotropic drug use. Soc Sci Med 1978; 12, 179-86.

NR979 Thursday, May 25, 12:00 PM - 2:00 PM

Urban and Rural Differences in Depression and Anxiety Disorders in Canada 2002

Sarah E. Romans, M.B. *University of Toronto, Centre for Research in Women's Health, 790 Bay Street, 7th Floor, Toronto, ON, M5G 1N8, Canada,* Marsha M. Cohen, M.D., Tonia Forte, M.S.C.

Educational Objectives:

At the end of this presentation, the participant will be able to describe how the modest increase in depression rates in urban over rural residents in Canada in 2002 was fully explained by differing socio-economic conditions in each locale.

Summary:

Objective: To examine differences in rates of 12-month depression and anxiety disorders among urban and rural (UR) dwellers in Canada.

Method: Data were from the 2002 Canadian Community Health Survey 1.2. Included were 31,321 respondents aged 15-69. We analyzed differences in the prevalence of depression and three anxiety disorders (agoraphobia, panic disorder, social phobia) across UR residence using Chi-square test ($p < 0.05$). Logistic regression was used to examine if UR differences in psychiatric disorders could be explained by socio-demographic, health and social variables.

Results: Bivariate analysis showed a modest difference in depression rates for urban versus rural dwellers (5.4 versus 4.3%, p=0.03). The urban-rural difference in the rate of depression was no longer significant (OR: 1.04; 95% CI: 0.80, 1.36) after adjusting for socio-demographic, health and social variables. No significant differences in rates of agoraphobia, panic disorder and social phobia by UR residence were found.

Conclusions: The UR demographic continues to generate theoretical interest, as we try to better understand how social environments affect health. These results suggest that any inherent UR differences in generating social capital are explained by socio-economic differences. Internal migration, which enables people to seek out the environment most conducive to their health, may play a role.

References:

1. Paykel E, Abbott R, Jenkins R, Brugha T, Meltzer H: Urban-rural mental health differences in Great Britain: findings from the National Morbidity Survey.Int Rev Psychiatry 2003;15(1-2):97-107.
2. Wang JL: Rural-urban differences in the prevalence of major depression and associated impairment. Soc Psychiatry Psychiatr Epidemiol 2004; 39(1):19-25.

NR980 Thursday, May 25, 12:00 PM - 2:00 PM

ADHD in Boys: Differences in Co-Morbidity Among Pediatric, Child Psychiatry, and Pediatric Neurology Clinics

Eugenio M. M. Rothe, M.D. *University of Miami, Div. of Child and Adolescent Psychiatry, 275 Glenridge Road, Key Biscayne, FL, 33149-1311*

Educational Objectives:

1) The attendee will be able to understand the importance of comorbidity in the diagnosis and treatment of ADHD

2) Will be able to understand the differences of comorbidity of ADHD among boys treated in Pediatric, Psychiatric and Pediatric Neurology Clinics

3) Will be able to understand differences in comorbidity of ADHD associated with public vs. private clinics, low SES vs. higher SES, Hispanic vs. African-American

Summary:

Abstract:

Objectives: Studies have shown that two thirds of children with ADHD are treated by primary care physicians (PCP), yet few studies have examined the differences in co-morbidity of ADHD between children treated by PCP and those treated by psychiatrists.

This study examines the differences in co-morbidity among one psychiatric and two pediatric outpatient populations. **Methods:** Boys ages 7 to 14 years old with a diagnosis of ADHD were chosen from three clinics in a county hospital: a child psychiatry clinic (n = 50), general pediatrics (n = 24), and an ADHD specialty clinic in the department of pediatrics (n = 11). The parents completed the Child Symptom Checklist (CSI), the Child Behavioral Checklist-Parent Rating Form (CBCL), and a demographic questionnaire. **Results:** One-way ANOVAs for the CSI variables showed significant differences for conduct disorder, major depression and GADs among the clinics. Post-hoc tests revealed that children in the psychiatric sample were more conduct disordered and more anxious than children in the general pediatrics clinic and were more depressed than the children in the ADHD specialty clinic. No differences were found on the CBCL scales. A chi-square test revealed that children in the psychiatric clinic were more likely to be on psycho-stimulants or taking two or more drugs and the children from the pediatric clinic were more likely to be on other types of drugs. Significant differences in co-morbidity were also found when comparing public versus private clinics, low SES versus high SES, and Hispanic versus African-American samples.

References:

1. Bennett FC, Sherman R. Management of childhood ƒhyperactivity§ by primary care physicians. J Dev Behav Pediatr (1983) 4:88-93.
2. Brown RT, Freeman WS, Perrin JM, Stein MT, Amler RW, Feldman HM, Pierce K, Wolreich ML. Prevalence of attention deficit / hyperactivity disorder in primary care settings. Pediatrics (2001) 107:1-11.

NR981 Thursday, May 25, 12:00 PM - 2:00 PM

A Structured Group Psychotherapy Program Improves Adjustment Tolipodistrophy in HIV-Positive Patients: A Pilot Study

Araceli Rousaud, Psy.D. *Hospital Clinic, Psychology department. IDIBAPS. Hospital Clinic de Barcelona, Villarroel 170, Barcelona, 08036, Spain*, Jordi Blanch, Ph.D., Anna Torres, Psy.D., Josep Maria Peri, Ph.D., Esteban Martinez, Ph.D., Manel Salamero, Ph.D., Josep Maria Gatell, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to demonstrate the efficacy of a structured time-limited cognitive-behavioral group psychotherapy program in improving adjustment to lipodistrophy in HIV-1 infected patients.

Summary:

Objective: To evaluate the immediate efficacy of a specific group therapy program in improving quality of life and adjustment to body changes due to fat redistribution (lipodistrophy syndrome) in HIV+ patients taking antiretroviral treatment. **Methods:** The therapy program consisted of 12 weekly two-hour sessions following a structured cognitive-behavioral group psychotherapy program focused on development of coping strategies, including specific psychoeducational interventions in nutrition and physical exercises. Eight HIV-positive patients with generalized lipodistrophy (affecting face, button and extremities) who referred psychological impairment due to body changes participated in a group therapy. Repeated measures Friedman test was used to analyse changes on the modified version of the Dermatological Quality of Life Inventory (DQLI) administered at three time points: T1 (one month before therapy), T2 (first session), and T3 (last session) **Results:** All participants (six women, and two men) completed the therapy program. A significant improvement was observed during the intervention time (between T2 and T3). No changes were observed during baseline (between T1 and T2). Issues raised by group participants were problems with dressing, fear of stigmatization, social isolation, and difficulties in sexual relations. **Conclusions:** Preliminary data show that our psychotherapy program improves quality of life and psychological adjustment to lipodistrophy body changes in HIV infected patients. Further groups should be performed to confirm its efficacy.

References:

1. Blanch J, Rousaud A, Hautzinger M. Assessment of the efficacy of a cognitive-behavioural group psychotherapy pro-

gramme for HIV-infected patients referred to a consultation-liaison psychiatry department. Psychother Psychosom. 2002 ; 71:77-84.

2. Bock J, Escobar-Pinzon LC, Riemer D, Blanch J, Hautzinger M. [EUROVIHTA Project--specific intervention program for HIV infected patients to support the coping process with this chronic illness] Psychother Psychosom Med Psychol. 2003l;53(7):310-318.

NR982 Thursday, May 25, 12:00 PM - 2:00 PM

Efficacy and Safety of Bupropion XL in Elderly Patients With Major Depressive Disorder

Roger Rousseau, M.D. *Aurora Clinical Trials, Neurosciences, 7800 SW 87th Avenue, Suite B250, Miami, FL, 33173*, Karen Hewett, Zoran Antonijevic, Donna Wightman, R.Ph., Jack G. Modell, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should understand the efficacy and safety of bupropion XL in the treatment of major depressive disorder in elderly patients.

Summary:

Introduction: Bupropion has consistently demonstrated safety and efficacy in the treatment of adults with MDD and demonstrated comparable safety and antidepressant efficacy in the elderly in a small study comparing bupropion Sustained Release with paroxetine. Large-scale, multi-center, placebo-controlled trials in the elderly, however, were lacking.

Methods: This 10-week, randomized, double-blind, placebo-controlled, multi-center, flexible-dose trial evaluated the efficacy and safety of bupropion XL (150-300 mg once daily) in 420 elderly outpatients (aged ≥ 65 years) with moderate-severe MDD. Efficacy measures included the MADRS and CGI scales.

Results: Bupropion XL demonstrated significant antidepressant efficacy over placebo as measured by mean change from baseline in MADRS total score (-16.6 versus -13.6, respectively, observed cases [OC]) ($p < .001$), mean change from baseline in reported sadness (LOCF and OC) ($p \leq .018$), and proportion of MADRS and CGI responders (LOCF and OC) ($p \leq .014$). While the protocol-defined primary endpoint, mean change in MADRS total score (LOCF), did not reach statistical significance ($p = .085$), this was largely due to outliers. The rank analysis of covariance, which more robustly adjusts for outliers, was statistically significant in favor of bupropion XL ($p = .033$). Bupropion XL was generally well tolerated with a safety profile broadly similar to that of placebo. No adverse events were reported for bupropion XL at a rate of ≥ 5% and at least twice the placebo rate. Discontinuations due to AEs (bupropion XL 8%, placebo 10%) and incidences of serious AEs (bupropion < 1%, placebo 3%) were low, and clinically significant changes in vital signs were reported at similar rates in the bupropion XL and placebo groups.

Conclusions: Bupropion XL demonstrated efficacy and safety in the treatment of elderly patients with MDD.

Supported by funding from GlaxoSmithKline

NR983 Thursday, May 25, 12:00 PM - 2:00 PM

Patients' Acceptance and Emotional Reactions to Disclosure of BPD Diagnosis

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the consequence for the patient to disclose the boderline personality disorder (BPD). The participant would be able to acknowledge that disclosing the BPD diagnosis can lead to a better acceptance of the diagnosis.

Summary:

Objective: This study examines responses to receiving the BPD Diagnosis and how this is related to: i) prior knowledge about the disorder; ii) information received during the diagnostic disclosure, and iii) attitude about proposed treatment.

Method: A semistructured interview was used to assess acceptance, reactions, knowledge, and intention to comply in 30 treatment-seeking BPD subjects who had received the BPD diagnosis within the month prior to the interview.

Results: Acceptance of the diagnosis was high. The general reaction was tending to feel better after the disclosure, and subjects felt more hopeful. Reactions for feeling ashamed or the self-esteem was not following a particular tendency. There was neither any relation found between patients' overall reaction to the diagnosis and the acceptance of the diagnosis, nor between the acceptance and the specific reactions (hopefulness, shame, self-esteem). Patients who have been previously treated for an axis I disorder were more likely to show more positive feeling than firstly diagnosed patients. Patients were significantly more likely to report intent to comply with a proposed treatment plan if they agreed with the diagnosis.

Conclusion: These results indicate that disclosure of the BPD diagnosis is more welcome than usually thought in clinical practices. More work is needed to overthrow the often-pejorative attitude towards the BPD diagnosis disclosure.

References:

1. Hoffman, P.D., Buteau, E., Hooley, J.M., Fruzzetti, A.E., Bruce, M.L.: Family members' knowledge about borderline personality disorder: correspondence with their levels of depression, burden, distress, and expressed emotion. Family Process 2003; 42:.

2. McDonald-Scott, P., Machizawa, S., Satoh, H.: Diagnostic disclosure: a tale in two cultures. Psychological Medicine 1992; 22: 147-157.

NR984 Thursday, May 25, 12:00 PM - 2:00 PM

Lamotrigine Therapy in Elderly Patients With Bipolar Disorder, Epilepsy, or Dementia

Martha Sajatovic *University Hospital Cleveland, 11100 Euclid Avenue, MS 5080, Cleveland, OH, 44106*, Kevin Nanry, Thomas Thompson

Educational Objectives:

At the conclusion of this presentation, the participant should be able understand patient response and tolerability to lamotrigine treatment.

Summary:

Objective: In spite of wide clinical use, there is a paucity of data on anticonvulsant drugs in elderly patients with psychiatric and neurological disorders. The authors conducted a systemized analysis of the literature on lamotrigine (LTG) therapy in elderly patients with BD, epilepsy, or dementia.

Methods: The search included electronic databases, meeting abstracts and presentations.

Results: Fourteen reports included controlled trials, retrospective analyses, and case studies. Reports of LTG in geriatric BD suggest improvement in depression, core manic symptoms and

delay in mood relapse. Mean dose in larger samples was 182-240 mg/day.[1,2] Controlled trials in geriatric epilepsy demonstrated efficacy and tolerability comparable to Gamma-aminobutyric acid pentin. Compared to carbamazepine, there were fewer treatment withdrawals and fewer cases of somnolence or rash in the LTG group. Preliminary reports in dementia note improvement in cognition, agitation and depression. While elimination of LTG can be affected by increasing age, disposition is more directly impacted by concurrent anticonvulsant therapy. There is extensive variability in LTG concentration/dose (C/D) ratios across the age-span, but as a group C/D ratios increase through adulthood.

Conclusion: LTG appears effective and was well tolerated in older adults with BD, epilepsy and dementia. Incidence and severity of adverse events appears similar to that established in younger patient populations.

This review was supported by GlaxoSmithKline.

References:

1. Sajatovic M. Maintenance treatment outcomes in older patients with bipolar I disorder. Am J Geriatr Psychiatry 2005;13(4):305-11.
2. Marcotte DB. Long-term use of lamotrigine for bipolar disorder in patients over 55 years of age. Poster presentation at the 157th Annual Meeting of the American Psychiatric Association, New York, NY, May 1-6, 2004.

NR985 Thursday, May 25, 12:00 PM - 2:00 PM

Cognitive Impairment in Patients With Chronic C Hepatitis

Francisco Sánchez, M.D. *Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Gastroenterology-Neurology and Psychiatry, Cuauhtemoc 46, Col Toriello-Guerra, Tlalpan, Mexico City, 14050, Mexico*, Maricarmen Flores-Miranda, M.S., Natasha Alcocer, M.D., Sandra Juárez, Psy.D., Graciela Castro-Narro, M.D., Aldo Montaño, M.D., Misael Uribe, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to know that cognitive disturbances are common in patients with chronic C hepatitis.

Summary:

Background: Disturbances in cognitive functions have been described in patients with chronic hepatitis, this could be explained by viral replication in the CNS. The presence of porto-systemic shunts related to chronic cognitive changes have been described in patients with significant liver impairment.

Objective: Determine the frequency and type of cognitive disturbances in patients with chronic C hepatitis.

Methods:

Design: Cross Sectional study

Setting: A tertiaty care referral center

Patients: One hundred and seventy patients, candidates to receive treatment with interferon alpha 2b and ribavirine were referred from the Hepatology clinic for psychiatric and cognitive evaluation. At the present moment 48 patients have completed the study.

Interventions:All patients have completed the neuropsychological test NEUROPSI, which evaluates orientation, reading/writing, attention/concentration, language, immediate memory, short time memory, executive functions. This test has been validated in Mexican population.

Main outcome measure: Cognitive disturbances

Results: Frequencies are described: reading/writing 8.4%, attention/concentration 37.5%, language 31.4%,immediate memory 39.7%, short time memory 48.2%, executive functions 80%.

Conclusions: Attention disturbances had been described in other studies, these could explain the memory disturbances found. Impairments in executive functions have not been described elsewhere. It is interesting and important to know that these cognitive disturbances might be related to central infection with the virus .

References:

1. Ortiz M. Córdova et al: Neuropsychological impairment in cirrhosis, include learning impairment. Journal of Hepatology 2005; 1727 9/7: 1-7.
2. Ortiz et al. Minimal Hepatic Encephalopathy. Diagnosis, Clinical significance and recommendations. Journal of Hepatology 2005;42: S45-S53.

NR986 Thursday, May 25, 12:00 PM - 2:00 PM

Dementia Rating Scale Differs on Late-Onset and Early-Onset Geriatric Depression

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Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the differences on cognitive performance between late-onset and early-onset geriatric depression.

Summary:

Introduction: Executive dysfunction was reported in elderly with late-onset depression. Little is known about cognitive differences between late-onset and early-onset geriatric depression, and the effects of treatment on cognitive functioning in the elderly.

Purpose: To compare the Mattis Dementia Rating Scale (MDRS) scores between late-onset and early-onset geriatric depression before and after treatment.

Methods: Forty-eight patients aged 60 and over were assessed with the MDRS before and after treatment for major depression (per DSM-IV) in a Geriatric Psychiatry Day Hospital program at Baycrest Hospital. Patients with dementia, other psychiatric or neurological disorders were excluded.

Results:

Twenty-three patients with late-onset and 25 with early-onset depression were assessed. The results showed improvement in depression (per HRSD) after treatment ($F(1,3)=50.103$, $p<0.001$), without difference between groups ($F(1,3)=0.013$, $p=0.911$).

Two-way analysis of co-variance, after controlling for first language and HRSD scores, showed that late-onset and early-onset depression groups differed on the initiation/perseveration ($F(1,7)=10.345$, $p=0.002$) and attention ($F(1,5)=5.50$, $p=0.022$) domains of the MDRS. The changes, however, did not vary across time (Initiation/perseveration: $F(1,7)=0.077$, $p=0.782$; Attention: $F(1,5)=1.09$, $p=0.300$).

Conclusions: In comparison to recurrent depression, late-onset depression had poorer performance on Initiation/perseveration but better performance on Attention per MDRS, with no significant group difference across time. Recurrent depression and depression with onset in late-life seem to affect cognition differently.

References:

1. Rapp MA, Dahlman K, Sano M, Grossman HT, Haroutunian V, Gorman JM. Neuropsychological differences between late-onset and recurrent geriatric major depression. Am J Psychiatry 2005; 162: 691-698.
2. Butters MA, Whyte EM, Nebes RD, Begley AE, Dew MA, Mulsant BH et al. The nature and determinants of neuropsychological functioning in late-life depression. Arch Gen Psychiatry 2004; 61: 587-595.

NR987 Thursday, May 25, 12:00 PM - 2:00 PM

Behavioral Inhibition and Shyness in HIV-Positive Patients

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Educational Objectives:

At the conclusion of this presentation, the participant should have an understanding of:

(i) the concept of behavioral inhibition, its prevalence and manifestations in HIV-positive individuals.

(ii) the relationship of behavioral inhibition to other psychopathology in this population, in particular anxiety disorders.

Summary:

Background: Social inhibition is a risk factor for HIV progression, probably mediated by autonomic nervous system (ANS) activity. In contrast, *behavioral inhibition* (BI) and *shyness*, both associated with anxiety disorders, have not been studied in HIV disease.

Methods: As part of a validation study of self-report measures, 485 HIV+ adults were screened for cognitive impairment on the Mini Mental State Examination (MMSE) and the HIV Dementia Scale (HDS). 406 patients scored >24 on the MMSE and >9 on the HDS and were administered the MINI, Center for Epidemiological Studies Depression Scale, Alcohol Use Disorders Identification Test, Retrospective Self-Report of Behavioral Inhibition, and the Revised Cheek and Buss Shyness Scale, among others. The relationship between childhood BI, shyness, anxiety, and HIV status was examined.

Results: Of the 406 patients, 75% were female. Mean age was 33.5 years and mean duration of HIV diagnosis was 33.9 months. About half (51%) were on antiretrovirals at assessment. 14 % met criteria for an anxiety disorder. The most prevalent anxiety disorder was PTSD (5.7%), followed by agoraphobia (5.2%) and GAD (4.7%). Patients with an anxiety disorder had significantly higher BI ($p < 0.001$) and shyness ($p < 0.015$) scores than patients without; in particular patients with social anxiety disorder ($p < 0.001$) and panic disorder ($p < 0.015$) reported more BI. While women reported more shyness than men overall ($p < 0.02$), there were no gender differences in BI. Neither CD4 counts nor viral loads were significantly correlated with BI or shyness.

Conclusions: These data, in an HIV-positive sample, support previous findings of a relationship between BI and anxiety, specifically social anxiety and panic disorder. Further work is needed establish if this relationship is mediated by shyness, and whether like social inhibition in HIV, is in turn mediated by the ANS.

References:

1. Cole SW, Kemeny ME, Fahey JL, Zack JA, Naliboff BD. Psychological risk factors for HIV pathogenesis: mediation by the autonomic nervous system. Biol Psychiatry.

2. Kagan J, Reznick JS, Snidman N. The physiology and psychology of behavioral inhibition in children. Child Dev 1987; 58: 1459-1473.

NR988 Thursday, May 25, 12:00 PM - 2:00 PM

Resources for Mental Health Research Mentoring and Career Development

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Educational Objectives:

At the conclusion of this session, the participant should be able to

1. Recognize the growing crisis in geriatric mental health research
2. Identify the importance of focused mentoring activities in preparing the needed workforce
3. Detail issues involved in geriatric mental health career development

Summary:

Objective:

The mental health needs of the rapidly growing older population demand not only more geriatric psychiatrists and clinicians, but also more investigators and researchers to increase understanding of these illnesses.

Method:

The NIMH has funded a 4-year educational initiative to develop tools and resources to meet the educational needs of mentees, mentors and mentors-in-training in geriatric mental health. The objective is: 1) to create a sustainable mentoring education resource through offline and online enduring materials; 2) to develop a content clearinghouse offering tools to maintain, launch, and enhance career development; and 3) to help prepare the research workforce to address the scientific opportunity and public health need.

Results:

Year 1 focused on creating seed content for the Web site www.MedEdMentoring.org. The site includes slide presentations on grant writing and other skills; case studies focusing on mentor-mentee interactions and mock grant reviews; career autobiographies of senior mentors; downloadable slides; mentoring Q&A; and an extensive resources section. Live symposia, CD-ROMs, and publications are planned for year 2.

Conclusion:

This unique resource provides tools that can be used by research mentees, mentors, and mentors-in-training at different stages of career development. It is a significant step in helping to prepare the needed workforce.

Funding acknowledgement: This project has been funded with Federal funds from the National Institutes of Health, Department of Health and Human Services, under Contract No. HHSN278200444084C.

References:

1. Reynolds CF III, Gatz M: Research training in mental health and aging: the harvest is plentiful; the laborers, few. Am J Geriatr Psychiatry 2003; 11:267-270.

2. Bruce ML: Challenges to the transition to independent investigator in geriatric mental health. Am J Geriatr Psychiatry 2003; 11:356-359.

NR989 Thursday, May 25, 12:00 PM - 2:00 PM

Long-Term Effects of Rivastigmine in Patients With Traumatic Brain Injury With Cognitive Deficits: Results of a 26-Week, Open-Label Extension to a 12-Week, Double-Blind Study

Jonathan M. Silver *Lenox Hill Hospital, 1430 2nd Avenue, Room 103, New York, NY, 10021-3313*, Barbara Koumaras, Michael Chen, Ph.D., Ibrahim Gunay

Educational Objectives:

Educational Objectives: At the conclusion of this presentation the participant should be able to recognize that the use of rivastigmine may improve some cerebral deficits secondary to TBI.

Summary:

Background: Traumatic brain injury (TBI) is a significant medical problem in the US. A substantial number of individuals with a non-penetrating TBI have persistent cognitive deficits or other neuropsychiatric disorders, for which there are no currently approved treatments.

Objectives: Objectives of this open-label extension were to evaluate the safety and tolerability and efficacy of memory and attention of rivastigmine 3-12 mg/day in patients who completed the double-blind period.

Methods: This was a 26-week, open-label extension to a 12-week double-blind, placebo-controlled, multi-center pilot study assessing the safety and efficacy of rivastigmine 3-6mg/day in patients with non-penetrating TBI with persistent cognitive deficits. Eligible patients had injury at least one year prior to baseline.

Results: Of the 157 patients treated in the double-blind phase, 127 patients (85 males/42 females) entered the extension. Mean age was 37.4 (range 19-55); 90.6% were Caucasian. In those patients who had at least 25% impairment on the HVLT at baseline, statistically significant improvement from baseline was observed at endpoint; in CANTAB-RVIP mean latency; CANTAB Reaction time; and HVLT Total Trials 1-3. These data are consistent with results from the double-blind treatment period and further support the findings of treatment response in TBI patients with significant memory impairment.

Conclusion: These results suggest that the enhancement of central cholinergic activity associated with long term use of rivastigmine may improve a number of cognitive deficits secondary to TBI.

References:

1. Griffin SL, van Reekum R, Masanic C. A review of cholinergic agents in the treatment of neurobehavioral deficits following traumatic brain injury. J Neuropsychiatry Clin Neurosci. 2003;15:17-26.
2. Chen Y, Shohami E, Constantini S, et al. Rivastigmine, a brain-selective acetylcholinesterase inhibitor, ameliorates cognitive and motor deficits induced by closed-head injury in the mouse. J Neurotrauma. 1998;15:231-237.

NR990 Thursday, May 25, 12:00 PM - 2:00 PM

Validation of the Mindstreams Computerized Cognitive Battery in Multiple Sclerosis

Ely S. Simon, M.D. *NeuroTrax Corporation, Clinical Science, 492-C Cedar Lane, # 322, Teaneck, NJ, 07666*, Yermi Harel, Ph.D., Nava Appleboim, M.S., Glen M. Doniger, Ph.D., Mor Lavie, M.S., Anat Achiron, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to evaluate the construct and discriminant validity of a set of computerized cognitive tests in measuring cognitive impairment associated with multiple sclerosis (MS).

Summary:

Objective: To validate Mindstreams® (NeuroTrax Corp., NY) Computerized Cognitive Battery (MCCB) in comparison to the gold standard Neuropsychological Screening Battery for Multiple Sclerosis (NSBMS).

Methods: 58 randomly selected multiple sclerosis (MS) patients and 71 age-, gender- and education- matched healthy subjects were evaluated with the NSBMS and the MCCB. The MCCB is a new computerized testing system that has been validated in mild cognitive impairment. It assesses verbal and non-verbal memory, executive function, visual spatial orientation, verbal function, attention, information processing speed, and motor skills and measures both accuracy and response time (RT).

Results: MCCB demonstrated good construct validity in comparison to the NSBMS in memory (r>0.42, p<0.001), executive function (r=0.55, p<0.001), attention (r>0.38, p<0.05), and information processing (r>0.35, p<0.05) domains. In addition, it demonstrated exceptional discriminant validity across a wide range of cognitive domains, most prominently executive function, attention, and motor skills (p<0.001). Additionally, MCCB RTs in all cognitive domains were longer in MS patients and varied with cognitive load, demonstrating that RT deficit in MS is associated with particular task demands.

Conclusions: MCCB is sensitive for detecting cognitive impairment in MS and has high construct validity relative to the NSBMS. MCCB also provides additional information, demonstrating prolonged RTs in cognitive performance in MS. Similar to prolonged latencies in evoked potentials, these findings suggest that even when accuracy on cognitive tests is within the normal range, there is prolonged conduction within demyelinated axons.

References:

1. Dwolatzky T, Whitehead V, Doniger GM, Simon ES, Schweiger A, Jaffe D, Chertkow H: Validity of a novel computerized cognitive battery for mild cognitive impairment. BMC Geriatr 2003; 3:4.
2. Hausdorff JM, Doniger GM, Springer S, Yogev G, Simon ES, Giladi N: A common cognitive profile in elderly fallers and in patients with Parkinson's disease: the prominence of impaired executive function and attention. Exp Aging Res 2006.

NR991 Thursday, May 25, 12:00 PM - 2:00 PM

Gender-Related Differences of Brain Function During a Selective Attention Task: An fMRI Study in Depressives and Healthy Volunteers

Thomas Sobanski, M.D. *Thueringen-Klinik Saalfeld-Rudolstadt, Psychiatry and Psychotherapy, Rainweg 68, Saalfeld, 07318, Germany*, Gerd Wagner, Ph.D., Georgios Sofianos, M.D., Natascha Bischoff, Ph.D., Eckart R. Straube, Ph.D., Heinrich Sauer, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to discuss gender-related differences of brain function in depressive patients and normal control subjects. The presentation will be focused on differences of brain activity assessed by functional magnetic resonance imaging during a selective attention task.

Summary:

Introduction: The aim of the present study was to assess gender-related differences of cerebral activity in major depression.

Methods: Functional magnetic resonance tomography (fMRI) scans were performed in a group of 16 inpatients with major depression (8 males and 8 females) and a control group matched for age and gender. fMRI scans were assessed by block design during neurocognitive stimulation with a selective attention pradigm. Data were analyzed by the SPM99 software.

Results: Healthy women showed stronger activations compared to healthy men in the visual cortex (BA 17, 18, 19), ventrolateral prefrontal cortex (VLPFC, BA 44), and circumscribed areas of the temporal and parietal lobes. Depressive Women showed less additional activations compared to depressive men predominantly located in the VLPFC (BA 44). Vice versa, healthy and depressive males exhibited only few extra activations compared to females. Selective attention task performance did not differ within the four groups.

Conclusions: Females used different strategies to perform the paradigm or it might have taken them a stronger effort. In depressive females the ability to generate additional activations pos-

sibly was limited. The results demonstrate that gender-related effects should be considered as a variance factor in future neuroimaging studies in major depression.

References:

1. Posener JA, Wang L, Price JL, Gado MH, Province MA, Miller MI, Babb CM, Csernansky JG: High-dimensional mapping of the hippocampus in depression. Am J Psychiatry 2003; 160:83-89.
2. Straube ER, Bischoff N, Nisch C, Sauer H, Volz HP: Input dysfunction and beyond - an evaluation of CPT components. Schizophr Res 2002; 54:131-139.

NR992 Thursday, May 25, 12:00 PM - 2:00 PM

Characteristics of Internet Addiction in Relation With Game Genre

Moon-Soo Lee *Seoul*, Hyoung-Seok Song, M.D., Min Nam, M.D., In-Kwa Jung, Sook-Haeng Joe, Seung-Hyun Kim, M.D., Hyeon-Soo Lee

Educational Objectives:

At the conclusion of this presentation, the participants should know that adolescents who play mainly different game genre can have different internet addiction potentials. Game and internet addictions shares many characteristics in common. Internet addiction high risk group also showed more game-play time, and tended to think that they have problems in self-control of game and computer use patterns. These characteristics can be related with low-self esteem, inadequate self-confidence and problematic interpersonal relationship patterns. We need understandings for addiction and interventions for inappropriate use of internet and games.

Summary:

Purpose

Some game genre is regarded as having greater addiction potentials than other game genre. At the same time, internet addiction cases are also rapidly increasing. Game and internet is very closely related. So we investigated games frequently used by adolescents and classified each games according to rule used popularly. We also examined the internet using patterns and tried to look for the relationships between game genre and internet using patterns.

Method

Participants were selected from middle school and high school which is located in eastern area of Seoul. Total 627 students (male 488, female 139) completed questionnaires composed of inquiry for computer and game using patterns and Korean internet addiction scales. Game genre was divided into 8 criteria (simulation, Role playing game, web-board, community, action, adventure, shooting, sports). We used a questionnaire inquiring game using patterns and Korean internet addiction scale.

Results

Using Korean internet addiction scales, 627 participants were divided into normal group (474), potential risk group (128) and high risk group (25). Male students spent significantly much time than female students for gaming. There was also significant differences in game playing time among different internet user groups. Each genre users group also showed significant differences in total internet addiction score and subscale scores.

RPG game users showed significantly higher internet addiction scores than other web-board, sports game users, and they had higher tendencies for virtual interpersonal relationship.

Conclusion

The results indicated that adolescents who play mainly different game genre can have different internet addiction potentials. Game and internet addictions shares many characteristics in common. Internet addiction high risk group also showed more game-play time, and tended to think that they have problems in self-control of game and computer use patterns. These characteristics can be related with low-self esteem, inadequate self-confidence and problematic interpersonal relationship patterns.

References:

1. Shapira NA, Goldsmith TD, Keck PE, Jr., Khosla UM, McElroy SL. Psychiatric features of individuals with problematic intertnet use. J Affect Disord 2000; 57:267-72.
2. Young KS. Pschology of computer use: XL. Addictive use of the internet: a case that breaks the stereotype. Psychol Rep 1996;79:899-902.

NR993 Thursday, May 25, 12:00 PM - 2:00 PM

NPI Subscale Analysis of Memantine/Donepezil Treatment in Moderate-to-Severe Attention Deficit

Pierre N. Tariot, M.D. *University of Rochester, Monroe Hospital, 435 East Henrietta Road, Rochester, NY, 14620,* Jeffrey L. Cummings, M.D., Jason T. Olin, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the potential for memantine to provide specific benefits for mood- and psychosis-related behavioral symptoms in AD.

Summary:

Objective: Memantine, a moderate affinity, uncompetitive N-methyl-D-aspartate (NMDA) receptor antagonist, is approved in the U.S. and in Europe for the treatment of moderate to severe Alzheimer's disease (AD).To assess the effects of memantine on behavioral disturbances in AD, a post hoc analysis of behavioral outcomes from a previously published trial of memantine in moderate to severe AD patients receiving stable donepezil treatment was performed.

Methods: Neuropsychiatric Inventory (NPI) individual items were aggregated into four subscales based on a modification to a previously reported factor analysis. Subscales were defined as follows: **Mood** (depression/dysphoria, anxiety, irritability/lability, night-time behavior disturbances, appetite/eating change), **Psychosis** (delusions, hallucinations, agitation/aggression), **Frontal** (euphoria/elation, disinhibition), or **Other** (apathy, aberrant motor behavior). The efficacy analysis was based on the Intention to Treat population, using the Last Observation Carried Forward approach to missing data.

Results: Baseline characteristics between the placebo treatment group and memantine treatment group were comparable. The total NPI score was significantly lower for the memantine group as compared to the placebo group at week 24 (P =.002), representing fewer behavioral disturbances and psychiatric symptoms in memantine-treated patients. On the Mood subscale, memantine/donepezil treated patients demonstrated improvement at study endpoint whereas placebo/donepezil treated patients worsened by 1.6 points (P=.002). Although symptoms of psychosis increased in both groups, the increase was significantly attenuated in memantine/donepezil treated patients compared to placebo/donepezil treated patients (P=.008). Frontal symptoms and Other symptoms were not significantly different between treatment groups.

Conclusions: These findings suggest that 6-months of memantine treatment in patients receiving stable donepezil significantly reduces behavioral symptoms in patients with moderate to severe AD, with a benefit for behaviors associated with mood and psychosis.

References:

1. Tariot PN, Farlow MR, Grossberg GT, et al. Memantine treatment in patients with moderate to severe Alzheimer disease already receiving donepezil: a randomized controlled trial. JAMA. 2004;291(3):317-324.
2. Frisoni GB, Rozzini L, Gozzetti A, et al. Behavioral syndromes in Alzheimer's disease: description and correlates. Dement Geriatr Cogn Disord. Mar-Apr 1999;10(2):130-138.

NR994 Thursday, May 25, 12:00 PM - 2:00 PM

Qualitative Evaluation of a Continuing Education Program Delivered by Telepsychiatry

John S. Teshima *University of Toronto, Psychiatry, 2075 Bayview Avenue, F-Wing, Toronto, ON, M4N 3M5, Canada*

Educational Objectives:

At the end of this presentation, participants will be able to:

1. List components of a continuing education program delivered by telepsychiatry that were particularly valued by its participants
2. List some of the challenges in delivering continuing education via telepsychiatry

Summary:

Objective: To identify successes and problems in a continuing education program delivered by telepsychiatry, by analysing completed evaluations.

Background: The Telepsychiatry Program in Toronto provides a continuing education program for staff at children's mental health centres across Ontario. The education program emphasises practical approaches and focuses on case presentations to engage participants and to encourage active learning.

Methods: All participants were asked to complete evaluation forms, which included prompts for written comments. Participant comments were qualitatively analysed for themes.

Results: Over 2000 evaluations were received by the end of 2004. A number of themes in the comments were highly recurrent, including: 1) the seminars were very relevant to the participants' practice; 2) information on management strategies was particularly valued; 3) case examples helped to illustrate concepts and enhance learning; and 4) interactive techniques, including role plays were useful. Additionally, a number of themes reflected the subjective impact of the seminars on the participants: 1) the seminars helped to reinforce existing knowledge; 2) the participants reflected more on their own practice; 3) and participants anticipated applying new knowledge to their own practices. These types of impacts are not often captured in the evaluation of education and highlight intermediate steps in the process of learning. Participants also wanted even more emphasis on practical strategies and case examples. Other concerns related to the numerous technological problems experienced over the course of these seminars. Challenges in the delivery of the education program included providing the same curriculum to many sites while at the same time accommodating the different learning needs of these sites.

Conclusions: Continuing education can be delivered successfully via videoconferencing to multiple and diverse distant sites. Seminars can be delivered according to the principles of effective continuing education and can still be experienced positively, despite some limitations with the technology.

References:

1. Allen M, Sargeant J, Mann K, Fleming M, Premi J: Videoconferencing for practice-based small-group continuing medical education: feasibility, acceptability, effectiveness, and cost. J Continuing Ed Health Prof 2003; 23: 38-47.
2. Hilty DM, Marks SL, Urness D, Yellowlees PM, Nesbitt TS: Clinical and educational telepsychiatry applications: a review. Canadian Journal of Psychiatry 2004; 49: 12-23.

NR995 Thursday, May 25, 12:00 PM - 2:00 PM

Mental Disorders in HIV-Infected Individuals Attending Various HIV-Treatment Sites in South Africa

Rita G. Thom, Prof. Dr. *University of the Witwatersrand, Psychiatry, 7 York Rd, Parktown, Johannesburg, 2193, South Africa*

Educational Objectives:

At the conclusion of this presentation participants will be able to discuss the findings of this new research, which is:

to determine the occurrence of mental disorders in patients attending various HIV-treatment sites in South Africa

and to compare this with the prevalence of mental disorders in the general population in South Africa and with similar studies in other countries.

Participants will also be able to discuss various ways of improving mental health care in HIV-treatment sites

Summary:

International studies show a significantly increased prevalence in mental disorders in HIV-infected individuals. Disorders range from neuropsychiatric disorders to anxiety and depressive disorders. Research conducted in Africa and South Africa in this area has been limited with some contradictory results.

Objectives:

To determine the occurrence of mental disorders in patients attending various HIV-treatment sites in South Africa

To compare this with the prevalence of mental disorders in the general population in South Africa and with similar studies in other countries.

Methodology:

This study was conducted at four sites: Three wellness clinics: in a large urban academic hospital, a rural hospital and an informal settlement), as well as the HIV clinic at Chris Hani Baragwanath Hospital. A semi-structured interview schedule was developed by the author to elicit risk and mitigating factors for mental disorders, and the Structured Clinical Interview for DSM (SCID: primary care, with psychotic screen version) was administered to 300 randomly selected and consented participants.

Results: Results of the first 150 interviews show that the occurrence of current mental disorders in this population is 30% with an additional 18% with V-codes. The lifetime prevalence of mental disorders is 32% with an additional 3% with V-codes.

Conclusions:

There is a high prevalence of mental disorders in people with HIV infection in this study. The results are comparable with similar studies in other countries. This is a selected sample and does not represent community samples of people with HIV infection in South Africa. This study was conducted during the first year of the roll-out of anti-retroviral treatment in South Africa. The majority of mental disorders detected are treatable with simple interventions such as anti-depressant medication, counselling, psychotherapy and social interventions. Mental health care should be an integral part of any HIV-treatment programme in South Africa.

References:

1. Morrison MF, Pettito JM, Ten Have T et al. Depressive and anxiety disorders in women with HIV infection. Am J Psychiatry. 2002 May;159(5):789-96.
2. Maj M, Janssen R, Starace F, Zaudig M, Satz P, Sughondhabirom B, Luabeya MA, Riedel R, Ndetei D, Calil HM, et al. WHO Neuropsychiatric AIDS study, cross-sectional phase 1. Study design and psychiatric findings. Arch Gen Psychiatry. 1994 Jan;51(1):39-.

NR996 Thursday, May 25, 12:00 PM - 2:00 PM

Clinical Response, Tolerability, and Cognition in Elderly Patients Treated With Lamotrigine

Thomas Thompson *GlaxoSmithKline, Psychiatry, 5 Moore Drive, MAI.C.2433, RTP, NC, 27709*, Jay Graham, Jeremy Roberts, Kevin Nanry

Educational Objectives:

At the conclusion of this presentation, the participant should be able understand patient response and tolerability to lamotrigine treatment.

Summary:

Objective: Depression and Bipolar Support Alliance reviewed the challenges to diagnosis and treat mood disorders in the elderly.[1] Clinical response, tolerability, and cognitive effects of lamotrigine were assessed as secondary endpoints in elderly patients from a large outpatient study.[2]

Methods: A post-hoc analysis was performed on a subset of patients (≥65 years old), who received open-label lamotrigine for 12 weeks to a target dosage of 200 mg/day. Measurements included the Clinical Global Impression Bipolar Version, Severity of Illness Scale (CGI-BP-S), the Clinical Global Impression Efficacy Index Scale (CGI-EI), and the Medical Outcomes Study Cognitive Scale (MOS-Cog). Analyses were performed using the last observation carried forward (LOCF).

Results: 47 patients were enrolled (Mean Age: 69.9 yrs; Gender: 59.5% female, 40.5% male). Mean (SD) CGI-BP-S overall scores were 3.1 (1.47) at baseline, 2.5 (1.29) at week 5 and 2.0 (1.12) at week 12. Per the CGI-EI, 80% of the study population at week 5 and 77% at week 12 reported the therapeutic effect of lamotrigine outweighed side effects. The mean (SD) change in the MOS-Cog score was 6.1 (19.96) from baseline to week 12. No serious rash was reported.

Conclusions: Mean CGI-BP-S and MOS-Cog scores improved or remained stable over 12 weeks when lamotrigine was added to current bipolar therapy with no serious rash reported.

This study was supported by GlaxoSmithKline.

References:

1. Charney DS, Reynolds CF, Lewis L et al. Depression and bipolar support alliance consensus statement on the unmet needs in diagnosis and treatment of mood disorders in late life. Arch Gen Psychiatry 2003;60:664-672.
2. Ketter TA et al. The Effect of Dermatologic Precautions on the Incidence of Rash with Addition of Lamotrigine in the Treatment of Bipolar I Disorder. J Clin Psych. In Press.

NR997 Thursday, May 25, 12:00 PM - 2:00 PM

Maintenance of Response to Memantine Treatment in Moderate to Severe Alzheimer's Disease Patients Receiving Stable Donepezil Treatment

Michael Tocco, Ph.D. *Forest Research Institute, Harborside Financial Center, Plaza V, 19th Floor, Jersey City, NJ, 07311*, Jason T. Olin, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participants should be able to recognize the value of maintaining memantine treatment based on measures of cognition, function, behavior and global measures.

Summary:

Objective: Memantine is a moderate affinity, uncompetitive NMDA receptor antagonist approved in the U.S. and in Europe for the treatment of moderate to severe Alzheimer's disease (AD). Post hoc analyses were performed using data from a previously conducted 24-week, double-blind, placebo-controlled trial of memantine (20 mg/day) in moderate to severe AD patients (N=404) treated with ongoing donepezil therapy (Tariot et al., 2004). These analyses assessed the maintenance of response on cognitive, functional, behavioral and global measures individually in a moderate to severe AD patient population.

Methods: The Severe Impairment Battery (SIB) was used to assess cognitive abilities. Functional and behavioral outcomes were measured with the Alzheimer's Disease Cooperative Study-Activities of Daily Living ($ADCS\text{-}ADL_{19}$) and Neuropsychiatric Inventory (NPI). Global status was assessed using the Clinician's Interview-Based Impression of Change Plus Caregiver Input (CIBIC-Plus). Maintenance of response for each outcome measure was defined as either no change or improvement above baseline scores for both weeks 12 and 24. Cochran-Mantel-Haenszel tests controlling for study center were performed on the Intention-to-Treat populations (OC and LOCF).

Results: Compared to patients receiving placebo, a significantly greater percentage of memantine-treated patients who responded at week 12 maintained their response at week 24 (OC analyses) on the SIB (52% versus 39.5%, P=.015), the $ADCS\text{-}ADL_{19}$ (36.6% versus 25.8%, P=.037), the NPI (50.9% versus 36.8%, P=.009), and the CIBIC-Plus for OC (48.5% versus 37.1%, P=.036). LOCF analyses yielded similar results, however maintenance of response on the CIBIC-Plus did not reach significance (P=.054).

Conclusions: These analyses indicate that, compared to placebo, a significant proportion of patients treated with memantine showed an early treatment response that was maintained for the duration of the 6-month study on all efficacy measures. These findings support the value of maintaining memantine treatment.

References:

1. Tariot PN, Farlow MR, Grossberg GT, et al. Memantine treatment in patients with moderate to severe Alzheimer disease already receiving donepezil: a randomized controlled trial. JAMA. 2004;291(3):317-324.
2. Schmitt FA, Ashford W, Ernesto C, et al.The severe impairment battery: concurrent validity and the assessment of longitudinal change in Alzheimer's disease.The Alzheimer's Disease Cooperative Study. Alzheimer Dis Assoc Disord.1997;11(Suppl 2):S51-S56.

NR998 Thursday, May 25, 12:00 PM - 2:00 PM

Health Services Utilization by Individuals With OCD From the UK Psychiatric Morbidity Survey of 2000

Albina R. Torres, M.D. *FMB -UNESP, Neurologia e Psiquiatria, Distrito de Rubião Jr., Botucatu (SP), 18618970, Brazil*, Martin J. Prince, M.D., Paul E. Bebbington, Ph.D., Dinesh Bhugra, Ph.D., Traolach S. Brugha, Ph.D., Michael Farrell, M.R.C., Rachel Jenkins, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to acknowledge that the majority of OCD cases in the community are not been treated, especially by mental health professionals. Comorbid cases are receiving significantly more treatment (both psychopharmacological and psychotherapeutic) than OCD cases with no comorbidity. Very few sufferers are receiving treatment approaches more specific and considered effective in OCD. Individuals with OCD that are in treatment may not be disclosing their obsessions and compulsions or not having these symptoms identified by the health professionals, prolonging the suffering and impairment associated with this condition.

Summary:

Background

Previous studies indicate that many individuals with OCD do not seek treatment for their problem. However, data from community samples in this area are scanty.

Aims

To analyse the use of health services in adults with OCD aged 16-74 years living in private households in the UK.

Method

Data from British National Survey of Psychiatric Morbidity of 2000, comprising 8,580 individuals, were analysed, comparing the use of health services by subjects with OCD and those with other neuroses, including possible differences between subtypes of OCD. All estimates were conducted with the weighted sample, using the Stata 8 software.

Results

One hundred and fourteen cases of OCD were identified, 76 with at least one additional neuroses. Over half (55%) had only obsessions, 34% obsessions and compulsions and 11% only compulsions. Compared to patients with other neuroses, OCD cases were more likely to be receiving treatment (40 versus 23%, $p<0.001$), mostly from GPs. However, only 9% had seen a psychiatrist and 5% a psychologist in the year before interview. Comorbid OCD cases were much more likely to be in treatment than "pure" cases (56% versus 14%), both psychopharmacological (50% versus 10%) and psychotherapeutic (28% versus 6%). Very few cases were receiving treatment approaches considered more effective for OCD. No differences in services use were found in cases with only obsessions, only compulsions or both kinds of symptoms.

Conclusions

The majority of OCD cases in the community are not been treated, especially by mental health professionals. Comorbid cases are receiving significantly more treatment than cases with no comorbidity. Individuals with OCD that are in treatment may not be disclosing their obsessions and compulsions or not having these symptoms identified by the health professionals, prolonging the suffering and impairment associated with this condition.

References:

1. Singleton N, Bumpstead R, O'Brien M, Lee A, Meltzer H: Psychiatric morbidity among adults living in private households, 2000. Int Rev Psychiatry 2003; 15(1-2):65-73.

2. Mayerovitch J I, duFort GG, Kakuma R et al. Treatment seeking for obsessive-compulsive disorder: role of obsessive-compulsive disorder symptoms and comorbid psychiatric diagnoses. Compr Psychiatry 2003; 44: 162-168.

NR999 Thursday, May 25, 12:00 PM - 2:00 PM

Personality Disorders Screen in OCD Cases From the UK Psychiatric Morbidity Survey of 2000

Albina R. Torres, M.D. *FMB -UNESP, Neurologia e Psiquiatria, Distrito de Rubião Jr., Botucatu (SP), 18618970, Brazil*, Martin J. Prince, M.D., Rachel Jenkins, Terry Brugha, Paul E. Bebbington, Glyn Lewis

Educational Objectives:

At the conclusion of this presentation, the participant should be able to acknowledge that positive screen for comorbid PDs occurs in the majority of OCD cases and some personality traits may be linked or even overlap with OCD symptoms. Personality psychopathology is the rule in OCD and should be routinely assessed, as it may affect help-seeking, diagnosis and treatment response.

Summary:

Background

Clinical studies indicate that most individuals with OCD have comorbid personality disorders (PDs), particularly from the anxious cluster. The prevalence of obsessive-compulsive (OC) personality disorder in OCD is still a controversial issue. There is a paucity of research in this area based on community samples.

Methods

Data from the British National Survey of Psychiatric Morbidity of 2000, comprising 8,399 adults were analysed, comparing the prevalence of positive screening for PDs in subjects with OCD, with other neuroses and non-neurotic controls, according to the self-report SCID-II. Within the OCD group we also analysed possible differences between genders and subtypes of the disorder. All estimates were conducted with the weighted sample, using the Stata 8 software.

Results

The prevalence for any PD in the OCD group (N = 108) was 74%, and 53% of them had multiple PDs, significantly more than both control groups. Paranoid, OC, avoidant, schizoid and schizotypal were the most common categories. Compared to other neurotics, OCD cases were more likely to have paranoid, avoidant, schizotypal, dependent and narcissistic PDs. Men were more likely to have PDs in general, cluster A PDs and antisocial, OC and narcissistic categories.

Conclusions

Positive screen for comorbid PDs was found in the majority of OCD cases. Cluster A and C PDs were the most common ones, with some characteristics that may be linked or even overlap with OCD symptoms. Personality psychopathology is the rule in OCD and should be routinely assessed, as it may affect help-seeking, diagnosis and treatment response.

References:

1. Singleton N, Bumpstead R, O'Brien M, Lee A, Meltzer H: Psychiatric morbidity among adults living in private households, 2000. Int Rev Psychiatry 2003; 15(1-2):65-73.

2. Bejerot S, Ekselius, von Knorring L. Comorbidity between obsessive-compulsive disorder (OCD) and personality disorders. Acta Psychiatrica Scandinavica 1998; 97: 398-402.

NR1000 Thursday, May 25, 12:00 PM - 2:00 PM

Guidelines for Laboratory Analysis and Application of Pharmacogenetic Testing to Clinical Practice in Psychiatry

Roland Valdes, Jr., Ph.D. *University of Louisville School of Medicine, Pathology and Laboratory Medicine, 511 S. Floyd Street, MDR Room 204, Louisville, KY, 40202*, Kristen K. Reynolds, Ph.D., Mark W. Linder, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to:

Recognize that evidence-based practice guidelines for pharmacogenetic (PGx) testing are being developed under the NACB (National Academy of Clinical Biochemistry) by expert laboratorians and clinicians from a variety of clinical specialties including psychiatry.

Understand the rationale for the development of practice guidelines for the application of pharmacogenetics (PGx) in the clinical setting.

Appreciate the complexities of developing evidence-based guidelines for optimizing the incorporation of pharmacogenetic considerations into psychiatric medication selection and dosing.

Suggest additional strategic recommendations relevant to clinical psychiatric practice to be included in the guidelines.

Summary:

Background: The application of pharmacogenetics (PGx) as a clinical adjunct to selection and dosing of drugs is relatively new and as such physicians, clinical laboratories, and regulatory agencies have not established evidence-based guidelines needed to optimize practice. Guidelines under development provide a framework for establishing optimum clinical utilization of PGx tests. *Objective*: The NACB is establishing guidelines for the use of PGx tests in various laboratory and clinical settings. The objective is to establish recommended approaches to guide the development and application of PGx as a discipline in clinical laboratory practice. Of interest to psychiatry is the selection of appropriate PGx testing profiles and the standards required for demonstration of clinical utility and efficacy. Examples are atomoxetine, aripiprazole, and many antidepressants metabolized by the polymorphic Cytochrome P4502D6 enzyme. *Approach*: An expert committee of physicians and clinical scientists is drafting evidence-based recommendations pertaining to several areas of focus including psychiatry. An external panel of experts will review a draft of the guidelines and a revised draft will be posted at www.nacb.org and also presented for open comments at various professional venues before final publication. Pharmacogenetics in psychiatry is of considerable interest because of the many psychiatric medications that are subject to pharmacogenetic variation, and the FDA's input on product labeling (including atomoxetine). Key issues related to utility in psychiatry will be documented and recommendations from attendants will be noted for assistance in guideline development. *Summary*: This new application derived from combining genetic testing with traditional psychopharmacology is rapidly evolving and as such the guidelines are likely to evolve rapidly. Nevertheless, these present guidelines will serve as a basis on which to establish a rigorous approach to define the applications of PGx to clinical practice and to provide the laboratory support needed to bring PGx to routine healthcare.

References:

1. Valdes R et al. Guidelines and Recommendations for Laboratory Analysis and Application of Pharmacogenetics to Clinical Practice. The National Academy of Clinical Biochemistry Laboratory Medicine Practice Guidelines 2006.
2. Spina, E et al. Metabolic drug interactions with new psychotropic agents. Fundam Clin Pharmacol 2003; 17: 517-538.

NR1001 Thursday, May 25, 12:00 PM - 2:00 PM

Divalproex Monotherapy and in Combination With Atypical Antipsychotics in the Management of Agitation and Aggression in Patients With Dementia

Mark R. Vanelli, M.D. *Adheris Inc, One Van DeGraff Drive, Burlington, MA, 05401*, Joan Hyde, Ph.D., Brent P. Forester, Lesley Adkison, R.N., Calixte Ahokpossi, M.A., Bill Sribney, Ph.D.

Educational Objectives:

To identify behavioral symptoms of dementia responsive to divalproex and to provide clinical guidance to physicians prescribing divalproex (Depakote ER and sprinkles) alone and in combination with atypical antipsychotics.

Summary:

Background: Behavioral disturbances in dementia are common and disabling to both patient and caregiver. Pharmacotherapy studies have been primarily limited to monotherapy trials. Studies are needed to provide clinical guidance under conditions of routine care, in which divalproex is often co-prescribed with atypical antipsychotics.

Objective: To identify behavioral symptoms of dementia responsive to divalproex and to provide clinical guidance to physicians prescribing divalproex (Divalproex Extended Release and sprinkles) alone and in combination with atypical antipsychotics.

Methods: This was a six week, open-label naturalistic pilot study of subjects recruited from a geriatric psychiatry inpatient unit, community assisted living and nursing home facilities. The primary outcome measure was the Cohen Mansfield Agitation Inventory (CMAI).

Results: Significant reductions were observed on the CMAI aggregate score at week 1 (-6.3, SE = 1.7, p<.00), week 3 (-8.2, SE = 1.8, p<.001), and week 6 (6.5, SE=2.4, p=0.02), and in the aggression subscale at week 3 (-3.0, SE=0.9, p=0.006) and week 6 (-3.1, SE=0.7, p=.002). At week 6, physically non-aggressive (-1.3, SE=0.9, p>.05) and verbally agitated behavior (-2.1, SE = 1.6, p>0.05) were not significantly improved.

Mean *divalproex* dose = 694 mg/day, mean serum level = 48.88 mg/L at week 6. Study sample included 8/12 men, mean age 81, mean MMSE score = 14.8. 7/12 subjects on combination therapy (5 quetiapine, 2 olanzapine). 10/12 on Divalproex Extended Release, 2/12 on Divalproex sprinkles. Divalproex was well tolerated with somnolence (3/12), gait disturbance (1/12) and thrombocytopenia (1/12) reported as adverse events at week 6 in 4/12 patients.

Conclusions: Interim results suggest divalproex may selectively help treat the physical aggression associated with dementia, but not verbal agitation and physical non-aggression (such as wandering). Divalproex doses and serum levels were lower than those used to treat bipolar disorder. Divalproex monotherapy and in combination with atypical antipsychotics was well tolerated.

References:

1. Porsteinsson AP & Tariot P et al: An open trial of valproate for agitation in geriatric neuropsychiatric disorders. An J Geriatr Psychiatry 1997; 5:344-351.
2. Lott AD, McElroy SL et al: Valproate in the treatment of behavioral agitation in elderly patients with dementia. J Neuropsychiatry Clin Neurosci 1995: 7:314-319.

NR1002 Thursday, May 25, 12:00 PM - 2:00 PM

Need and Utilization of Psychiatric Services Among General Hospital Inpatients

Johannes Wancata, M.D. *Medical University of Vienna, Department of Psychiatry, Wahringer Gurtel 18-20, Vienna, 1090, Austria*, Monika Krautgartner, M.D., Norbert Benda, M.D., Rainer Alexandrowicz, Ph.D.

Educational Objectives:

Readers of the poster will learn about the high prevalence of mental disorders in non-psychiatric general hospital settings. Based on principal considerations of service planning they will understand the guidelines developed by an expert group for the selection of patients who need psychiatric consultation. They will recognize that not each patient with psychiatric co-morbidity needs psychiatric interventions during hospital stay. The potential reasons for under-provision of psychiatric services will be understood from the results of an epidemiological survey among general hospital inpatients.

Summary:

Objective: The aim of the present study was to estimate the need for psychiatric consultation and psychiatric inpatient referral among non-psychiatric inpatients, and to assess the utilisation of these services. **Methods:** This study was carried out among 993 inpatients of medical, surgical, gynaecological and physical rehabilitation wards in Austrian hospitals. Psychiatric case-identification was performed by research psychiatrists using the Clinical Interview Schedule. Diagnoses were given according to DSM-III-R. The assessment of need for consultation and inpatient referral was based on guidelines. **Results:** Overall, 34.6% suffered from

some kind of psychiatric disorder. Of all cased, 43.3% needed consultation and 7.8% inpatient referral. Only 21.4% of the cases were actually seen by a consultation psychiatrist and 0.6% were referred to a psychiatric ward. Comparing the estimated need with the actually provided psychiatric consultations, only 33.3% of them had their need met. In contrast, a psychiatric consultation was performed among 5% of those not needing psychiatric services ("overprovision"). Using logistic regression analysis, variables of the health care system (i.e. department type and catchment area of the hospital) were among the predictors of the actual consultations. **Conclusion:** The rate of actual consultations and admissions to psychiatric wards was markedly lower than the need according to psychiatrists' judgment. Structural aspects of the health care system (e.g. psychiatric training of ward physicians, availability of medical staff, accessibility of psychiatric services) seem to predict the actual utilization of psychiatric services.

References:

1. Goldberg DP, Cooper B, Eastwood MR, Kedward HB, Shepherd M: A standardized psychiatric interview for use in community surveys. Brit J Prev Soc Med 1970; 24: 18-23.
2. Ortega AN, Mc.Quaid EL, Canino G, Ramirez R, Fritz GK, Klein RB: Association of psychiatric disorders and different indicators of asthma in island Puerto Rican children. Soc Psychiatry Psychiatr Epidemiol 2003; 38: 220-226.

NR1003 Thursday, May 25, 12:00 PM - 2:00 PM

Efficacy of Donepezil in Severe Alzheimer's Disease: Primary End Points of a Randomized, Double-Blind, Placebo-Controlled Study

Bengt Winblad, M.D. *Karolinska Institute, Neurotec, Karolinska University, Huddinge, B84, Stockholm, SE-141 86, Sweden*, Lennart Minthon, M.D., Sture Eriksson, M.D., Stellan Båtsman, M.D., Catarina Jansson-Blixt, Ph.D., Anders Haglund, Lena Kilander, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to appreciate the cognitive and functional benefits of donepezil treatment on those with severe AD.

Summary:

Objective: To investigate donepezil's efficacy and tolerability in patients with severe (Mini-Mental State Examination [MMSE] score: 1-10, and Functional Assessment and Staging Scale: 5-7c) Alzheimer's disease (AD).

Methods: A 6-month randomized, double-blind placebo-controlled study conducted at 50 centers in Sweden. Patients were randomized to receive donepezil 5 mg/day then 10 mg/day (n= 128) or placebo (n=120). Outcome measures were change from baseline to month 6 on the Severe Impairment Battery (SIB) and modified AD Cooperative Study ADL Inventory for Severe AD (ADCS-ADL-severe). The primary endpoints SIB and ADCS-ADL-severe were analyzed using a general linear model with overall treatment effect assessed by Type III sums of squares. All tests were performed at the 0.05 significance level and were 2-tailed. The efficacy analyses were conducted on the intent-to-treat (ITT) and the per protocol (PP) populations. Both last observation carried forward (LOCF) and observed cases (OC) were conducted.

Results: Baseline patient characteristics were similar between treatment groups. Mean screening MMSE scores at baseline (±SD) were 6.0±3.0 (donepezil; n=128) and 6.2±3.0 (placebo; n=120). Donepezil-treated patients showed greater mean improvement (SIB) and less mean decline (ADCS-ADL) than placebo. The between group difference was statistically significant for the SIB (LS mean change: 3.4 and -2.2 for donepezil and placebo groups, respectively; P=0.008, ITT-LOCF analysis) and the ADCS-ADL-severe (LS mean change: -1.4 and -3.0 for donepezil and placebo groups, respectively; P=0.029 ITT-LOCF analysis). Ninety-five (74.2%) donepezil- and 99 (82.5%) placebo-treated patients completed the study. The incidence of AEs was comparable between donepezil and placebo groups (82.0% versus 75.8%, respectively), the majority of which were mild or moderate in severity. Conclusion: Donepezil provided significant cognitive and functional benefits compared with placebo, in patients with severe AD.

Study grant from Pfizer AB

References:

1. Feldman H, Gauthier S, Hecker J, Vellas B, Xu Y, Ieni JR, Schwam EM; Donepezil MSAD Study Investigators Group: Efficacy and safety of donepezil in patients with more severe Alzheimer's disease: a subgroup analysis from a randomized, placebo-controlle.
2. Tariot PN, Cummings JL, Katz IR, Mintzer J, Perdomo CA, Schwam EM, Whalen E: A randomized, double-blind, placebo-controlled study of the efficacy and safety of donepezil in patients with Alzheimer's disease in the nursing home setting. J Am Geriatr S.

NR1004 Thursday, May 25, 12:00 PM - 2:00 PM

Efficacy of Donepezil on Secondary End Points in a Randomized, Double-Blind, Placebo-Controlled Study in Severe Alzheimer's Disease

Bengt Winblad, M.D. *Karolinska Institute, Neurotec, Karolinska University, Huddinge, B84, Stockholm, SE-141 86, Sweden*, Sture Eriksson, M.D., Lena Kilander, M.D., Stellan Båtsman, M.D., Catarina Jansson-Blixt, Ph.D., Anders Haglund, Lennart Minthon, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to appreciate the positive impact of donepezil treatment on those with severe AD.

Summary:

Objective: To evaluate donepezil's efficacy in cognition (Mini-Mental State Examination; MMSE), global function (Clinical Global Impression of Improvement; CGI-I), and behavior (Neuropsychiatric Inventory; NPI) in patients with severe Alzheimer's disease (AD).

Methods: This double-blind, multicenter study, conducted at 50 centers in Sweden, followed 248 patients with severe (MMSE score: 1-10 and Functional Assessment and Staging Scale: 5-7c) AD for 6 months. Patients were randomized to donepezil 5 mg/day then 10 mg/day (n=128) or placebo (n=120). The secondary outcome measures were cognition (MMSE), global function (CGI-I), and behavior (NPI); Cognition, global function, and behavior were evaluated by change from baseline to month 6 on each test. MMSE and NPI were analyzed using a general linear model with treatment effect assessed by Type III sums of squares. The CGI-I was analyzed using a Cochran-Mantel-Haenszel chi-square test. All tests were performed in the intent-to-treat (ITT) population at the 0.05 significance level and were 2-tailed.

Results: Baseline patient characteristics were similar between treatment groups. Mean screening MMSE scores at baseline (±SD) were 6.0±3.0 (donepezil; n=128) and 6.2±3.0 (placebo; n=120). At month 6, and versus placebo in each case, donepezil-treated patients showed greater LS mean improvements on the MMSE (P=0.009; ITT-OC and ITT-LOCF analysis); significantly more donepezil-treated patients were rated as very much improved, improved or minimally improved on the CGI-I, (P=0.008; ITT-OC analysis), and results almost reached significance favoring donepezil in the ITT-LOCF analysis (P=0.055); there were

no differences between the 2 groups on the NPI (P=0.43; ITT-LOCF).

Conclusion: When compared with placebo, donepezil showed significant benefits in cognition and clinical global function.

Study grant from Pfizer AB

References:

1. Feldman H, Gauthier S, Hecker J, Vellas B, Xu Y, Ieni JR, Schwam EM; Donepezil MSAD Study Investigators Group: Efficacy and safety of donepezil in patients with more severe Alzheimer's disease: a subgroup analysis from a randomized, placebo-controlle.
2. Tariot PN, Cummings JL, Katz IR, Mintzer J, Perdomo CA, Schwam EM, Whalen E: A randomized, double-blind, placebo-controlled study of the efficacy and safety of donepezil in patients with Alzheimer's disease in the nursing home setting. J Am Geriatr S.

NR1005 Thursday, May 25, 12:00 PM - 2:00 PM

Clinically Significant Cognitive Impairment in Older Adults Following Mild to Moderate Traumatic Brain Injury

Uri Wolf, M.D. *University of Toronto, 108 Frontenac Ave, Toronto, ON, M5N1Z9, Canada*, Mark J. Rapoport, M.D., Nathan Herrmann, M.D., Prathiba Shammi, Ph.D., Alex Kiss, Ph.D., Andrea Phillips, B.A., Anthony Feinstein, M.R.C.

Educational Objectives:

At the conclusion of this presentation the participant should be able:

1. To recognize the clinical significance of a mild to moderate TBI in older adults in terms of the risk of future development of MCI or AD.
2. To understand the limitations of self- and informant-report of cognition in a TBI population.
3. To appreciate the need for further research regarding long term cognitive outcomes following TBI in older adults.

Summary:

Objective: To determine whether mild to moderate Traumatic Brain Injury (TBI) in older adults increases the risk of developing Mild Cognitive Impairment (MCI) or Alzheimer's disease (AD) two years after injury.

Methods: Participants aged 50 or older, with mild-to-moderate TBI were compared with an age-, gender-, and, education-matched healthy control group on aspects of cognition in a longitudinal study. Cases were selected from the Extended Release and trauma wards in a regional trauma center (n=69). Healthy controls from the community were selected by response to advertisements (n=79). Forty-nine cases and sixty-eight controls were followed at one year and thirty cases and forty-six controls were followed at two years. Neuropsychological tests were administered at one and two years. At one and two years post injury, participants were blindly rated as MCI (Petersen criteria), AD (DSM-IV Criteria), or not impaired.

Results: Generalized Estimating Equation (GEE) models were run controlling for, age, gender, education, major depression, APOE genotype, and medical illness severity. There was no statistically significant difference in incidence of impairment (MCI or AD) between case and control at one year (12% versus 2%, respectively) or two years (10% versus 4%, respectively) following TBI.

Conclusions: Whereas previous studies show impairment in cognitive outcomes after mild to moderate TBI in older adults, this does not translate into an increased incidence of MCI or AD at one and two years post injury. MCI and AD are clinically relevant causes of cognitive impairment. These results suggest either that there are no clinically significant cognitive sequelae after mild to moderate TBI at two years after injury, or that MCI and AD do not adequately capture this outcome. As well, a larger sample may be necessary to detect a significant difference between groups.

References:

1. Luukinen H, et al: Fall related brain injuries and the risk of dementia in elderly people: a population-based study. Eur J Neurol 2005;12:86-92.
2. Jellinger KA: Head injury and dementia. Curr Opin Neurol 2004; 17: 719-723.

NR1006 Thursday, May 25, 12:00 PM - 2:00 PM

The Prevalence of Mental Health Problems in the Canadian Armed Forces: Comparison With the Canadian General Population

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Educational Objectives:

At the end of this session, the participant should understand the difference in the prevalence of common mental health problems in the Canadian Armed Forces compared to the Canadian general population.

Summary:

Background: Mental health problems (MHP's) can both result from and interfere with military service This study describes the prevalence and impact of MHP's in service members relative to the general population. **Methods:** Interviewers administered a health survey to a stratified random sample of 5,155 Regular Forces (RegF) members of the Canadian Forces and 36,984 members of the Canadian general population (overall response rates 80% and 77%, respectively). Regression analysis was used to compare the prevalence and impact of six MHP's that were assessed in both populations. **Findings:** The 12-month prevalence of any MHP in RegF members was 15.8%, and the 12-month prevalence of major depression was 7.9%. After correction for potential demographic confounders, the odds of the following problems were significantly greater in RegF members than in the general population: Any 12-month and any lifetime MHP (OR 1.3 [95% CI 1.2 - 1.5]; p<0.0001 and OR 1.2 [1. 1 - 1.3]; p=0.0001, respectively); 12-month and lifetime major depression (OR 2.1[1.8 - 2.5]; p<0.0001 and OR 1.7 [1.5 - 1.9]; p<0.0001, respectively), and 12-month panic disorder (OR 1.5 [1.1 - 2.0]; p=0.0110). RegF members with one or more 12-month MHP had greater perceived dysfunction and were also much more likely to have utilized mental health services (OR 2.0 [1.5 - 2.5]; p<0.0001) than their general population counterparts. **Interpretation:** Canadian RegF members suffer disproportionately from any of six common mental health problems and from major depression and panic disorder in particular. This may be due to toxic mental health effects of military service or to selection of vulnerable individuals.

References:

1. Hourani LL, Yuan H. The mental health status of women in the Navy and Marine Corps: preliminary findings from the Perceptions of Wellness and Readiness Assessment. Mil Med 1999 Mar;164(3):174-81.
2. Hoge CW, Lesikar SE, Guevara R, Lange J, Brundage JF, Engel CC, Jr., et al. Mental disorders among U.S. military personnel in the 1990s: association with high levels of health care utilization and early military attrition. Am J Psychiatry 2002 Sep;15.

NR1007 Thursday, May 25, 12:00 PM - 2:00 PM

Prevalence of Mental Health Problems in the Canadian Regular and Reserve Armed Forces: Exploration of Occupational Risk Factors

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Educational Objectives:

After attending this session, the participant will be able to:

1) Understand the lower prevalence of common mental health problems in the Canadian Regular Armed Forces vs. the Reserve Forces.

2) Understand the association between various occupational factors and the risk of mental health problems.

Summary:

Background: Regular Canadian Armed Forces (CF) members have a two-fold higher risk of depression than their general population counterparts. Exploration of the association of mental health problems with service-related factors provides insight into which aspects of military service might contribute to this excess prevalence. **Methods:** Interviewers administered a survey based on the Composite International Diagnostic Interview (CIDI) to a stratified random sample of 5,155 Regular and 3,286 Reserve Force members of the CF. Logistic regression was used to explore the association between self-reported occupational factors with the risk of any of eight lifetime (LT) mental health problems (MHP), LT depression, and LT PTSD. **Findings:** After correction for confounding factors, Reserve Force members had lower overall odds of any LT MHP (OR = 0.61; CI: 0.53 - 0.71, p < 0.0001), LT depression (OR = 0.45; CI: 0.37 - 0.56, p < 0.0001), and LT PTSD (OR = 0.57; CI: 0.41 - 0.80, p = 0.001). There was a positive trend for the association between the total number of career deployments with LT PTSD (OR for 2 to 3 deployments = 1.40; CI: 0.97 - 2.01, p = 0.074; OR for 4 or more deployments = 1.64; CI 0.95 - 2.81, p = 0.074) but not with any LT MHP or LT depression. Total time away from home in the previous two years was not an independent risk factor for any of the three primary outcomes. **Interpretation:** Canadian Reserve Force members have a lower risk of any LT MHP, LT depression, and LT PTSD than Regular Force members. The absence of an association between total number of career deployments and total time away from home in the previous two years with depression suggest that these are not the cause of its excess prevalence in the Regular Forces.

References:

1. Riddle JR, Smith TC, Smith B, et al. Prevalence of mental health morbidity in the US military: The baseline mental health of the Millennium Cohort; USA-CHPPM 8th Annual Force Health Protection Conference, Albuquerque, NM, August, 2005.
2. Hoge CW, Castro CA, Messer SC, McGurk D, Cotting DI, Koffman RL. Combat duty in Iraq and Afghanistan, mental health problems, and barriers to care. N Engl J Med 2004 Jul 1;351(1):13-22.

NR1008 Thursday, May 25, 12:00 PM - 2:00 PM

A Review of Patient-Reported Outcomes in Cognitive Impairment

Yang Zhao, Ph.D. *Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN, 46285*, Lori Frank, Ph.D., Leah Kleinman, D.P.H.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to summarize the patient-reported outcomes relevant to AD, and identify the important and valid instrument to be used in AD studies.

Summary:

Objective: Patient reported outcomes (PROs), such as health-related quality of life (HRQL), functional status, and health status have been widely used to measure the impact of cognitive impairment (CI) on the lives of patients and their caregivers. This study summarizes the characteristics of existing instruments and assesses their usefulness in measuring the impact of CI interventions on patients.

Methods: A literature review was conducted to identify existing PRO measures for CI. The psychometric characteristics of existing instruments were assessed.

Results: PRO measures for CI cover HRQL, basic activities of daily living (ADLs), instrumental ADLs, symptom severity and distress, behavioral disturbance, mood, and caregiver burden. Existing instruments provide valid measures for patient HRQL, some aspects of functioning, and affect (e.g., depression) for patients with mild to moderate CI. However, few data exist on treatment adherence, satisfaction or symptom distress. Randomized clinical trials (RCTs) have frequently included PROs to assess the efficacy of CI interventions, and the most emphasized impacts are on patient behavioral disturbance and functioning. Although minimal important differences (MIDs) have become important for interpretation of RCT data, no published clinical trials have reported MIDs for available PROs in CI. Conclusion: PROs are important to measure the impact of CI intervention. Existing PROs address a broad range of important concepts in CI, however, not all areas are adequately measured. Studies on MIDs for PROs in CI are needed to aid the interpretation of the data.

References:

1. Galasko D, Bennett D, Sano M, et al: An inventory to assess activities of daily living for clinical trials in Alzheimer's disease. The Alzheimer's Disease Cooperative Study. Alzheimer Dis Assoc Disord. 1997;11 Suppl 2:S33-39.
2. Trinh NH, Hoblyn J, Mohanty S, Yaffe K: Efficacy of cholinesterase inhibitors in the treatment of neuropsychiatric symptoms and functional impairment in Alzheimer disease: a meta-analysis. JAMA. 2003; 289:210-216.

NR1009 Thursday, May 25, 12:00 PM - 2:00 PM

Presurgical Psychiatric Screening of Bariatric Surgery Candidates: Frequency and Reasons for Exclusion

Mark Zimmerman, M.D. *Rhode Island Hospital, psychiatry, 235 Plain Street, Suite 501, Providence, RI, 02905*, Caren Francione-Witt, M.A., Daniela Boerescu, M.D., Dieter Pohl, M.D., Dean Roye, M.D., David Harrington, M.D., Iwona Chelminski, Ph.D.

Educational Objectives:

At the conclusion of this presentation the participant should be more familiar with the reasons for excluding patients from bariatric surgery.

Summary:

Background: Psychological factors can contribute to the cause of obesity; therefore, it has been recommended that presurgical candidates for bariatric surgery receive a psychiatric evaluation to determine their appropriateness for surgery. However, there are no clear guidelines for determining whether or not a patient is a poor candidate from a psychiatric perspective, and little infor-

mation on how many patients are not recommended for surgery and the reasons for the negative recommendation.

Method: Three-hundred candidates for bariatric surgery were interviewed with a semi-structured interview assessing patients' dietary habits, history of weight loss efforts, reasons for having the surgery, expectations regarding the surgery, and expectations regarding outcome. In addition, we administered a comprehensive semi-structured interview evaluating DSM-IV axis I and II disorders. Psychiatrists reviewed the results of the evaluation and completed the assessment by conducting an unstructured clinical interview.

Results: Twenty-one percent (n=62) of the patients were not recommended for surgery. The most common reasons for the negative recommendation were: overeating to cope with stress/ emotional distress (n=38), eating disorder (n=15), uncontrolled psychopathology at the time of the evaluation (n=10), and the presence of significant life stressors (n=7). No patients were excluded for a lack of understanding of the potential risks of surgery.

Conclusion: A significant number of applicants for bariatric surgery were not considered by psychiatrists to be appropriate surgical candidates at their initial screening evaluation.

References:

1. Black, D.W., Goldstein, R.B., & Mason, E.E. (1992). Prevalence of mental disorder in 88 morbidity obese bariatric clinic patients. American Journal of Psychiatry, 149 (2), 227-234.
2. Wadden, T.A., Sarwer, D.B., Womble, L.G., Foster, G.D., McGikin, B.G., & Schimmel, A. (2001). Psychosocial aspects of obesity and obesity surgery. Obesity Surgery, 81 (5), 1001-1025.

NR1010 Thursday, May 25, 12:00 PM - 2:00 PM

A Psychometric Evaluation of the *DSM-IV* Pathological Gambling Diagnostic Criteria

Mark Zimmerman, M.D. *Rhode Island Hospital, Psychiatry, 235 Plain Street, Suite 501, Providence, RI, 02905*, Diane D. Young, Ph.D., Iwona Chelminski, Ph.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to describe the psychometric properties of the DSM-IV pathological gambling criteria in psychiatric outpatients who screen positive for gambling problems.

Summary:

Background: Specific diagnostic criteria for pathological gambling (PG) have been available for twenty-five years, since the publication of DSM-III. Little research has examined the psychometric performance of the diagnostic criteria. The goal of the present report from the Rhode Island Methods to Improve Diagnostic Assessment and Services (MIDAS) project was to examine the sensitivity, specificity and predictive values of the DSM-IV PG criteria for psychiatric outpatients who screened positive for a gambling problem. **Methods:** One thousand seven hundred and nine psychiatric outpatients were evaluated with a semistructured diagnostic interview for PG. **Results:** Eighty-eight patients screened positive for PG, 40 of whom met DSM-IV diagnostic criteria for a lifetime history of PG. All ten DSM-IV criteria were significantly more frequent in the PG group. The sensitivity of the criteria ranged from 25.0% to 90.0% (mean=67.8%), whereas specificity ranged from 62.5% to 100% (mean=81.9%). Positive predictive values ranged from 64.1% to 100% (mean=78.9%), and negative predictive values ranged from 61.5% to 90.7% (mean= 77.1%). **Discussion:** Guidelines are recommended for determining whether a diagnostic criterion should be retained as part of the set of diagnostic criteria, and our results suggested that two of the DSM-IV PG criteria are candidates for elimination (criterion 8_commitment of illegal acts; criterion 10_reliance on others for financial assistance to relieve a desperate financial problem).

References:

1. Lesieur, H.R., Rosenthal, R.J. (1991). Pathological gambling. Journal of Gambling Studies, 4, 5-40.
2. Toce-Gerstein, M., Gerstein, D., Volberg, R. (2003). A hierarchy of gambling disorders in the community. Addiction, 98, 1161-1672.

NR1011

Flexible Dose Open Label Trial Evaluating the Efficacy and Safety of Quetiapine (Seroquel) as Adjunctive Pharmacotherapy for the Treatment of GAD

Martin A. Katzman, M.D.; Monica Vermani; Leslie Jacobs; Madalyn Marcus; S. Lessard; W. Galarraga; Brian Y. Kong; L. Struzik

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize atypical antipsychotics as a viable treatment option for treatment-resistant GAD.

Summary:

Generalized Anxiety Disorder (GAD) is one of the most common anxiety disorders with a lifetime prevalence of over 4%, and causes substantial interference with daily living. Despite the gamut of studied psychotropic medications available, many treatment resistant patients remain, requiring the development of new potential therapies, including atypical antipsychotics, such as Quetiapine.

The present study employs a 12 week open-label design to test the efficacy and safety of Seroquel as an adjunctive intervention to treatment-resistant GAD or non-remitted cases.

Patients (N = 31) who have completed treatment, their outcomes indicate statistically significant symptom reduction on measures of anxiety symptoms (HAM-A) from baseline to last observation carried forward ($t(30) = 11.84$, $p < 0.001$; 72% symptom reduction). There was also a significant decrease on the Penn State Worry Questionnaire ($t(25) = 5.80$, $p < 0.001$) and a significant improvement in sleep quality as assessed by the Pittsburg Sleep Quality Index (PSQI) ($t(18) = 8.25$, $p < 0.001$). Patients also reported a significant increase in the state of their current overall health ($t(29) = 4.34$, $p < 0.001$) and there was an increase in total Global Assessment Scale (GAS) score ($t(29) = 8.48$, $p < 0.001$). Symptom severity, as rated on the CGI, declined significant ($t(27) = 8.63$, $p < 0.001$). Work, social life/leisure activities, and family related disability improved post treatment ($t(29) = 4.20$, $p < 0.001$; $t(29) = 5.37$, $p < 0.001$; $t(29) = 3.77$, $p < 0.01$).

Although these results are preliminary, the addition of atypical antipsychotics to treatment-resistant GAD appears to be beneficial in symptom reduction and increasing quality of life.

References:

1. Massion AO, Warshaw Mg, Keller Mg. 1993. Quality of life and Psychiatric Morbidity in Panic Disorder and Generalized Anxiety Disorder. Am J Psychiatry, 150(4), 600-607.
2. Olfson M, Fireman B, Weissman Mm, Leon Ac. Sheehan Dv, Kathol Rg, Hoven C, Farber L. 1997. Mental Disorders and Disability Among Patients in a Primary Care Group Practice. Am J Psychiatry, 154(12), 1734-1740.

NR1012

Diagnostic and Treatment Differences in Children and Adults With ADHD

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Educational Objectives:

At the conclusion of this session, the participant should be able to:

1. Discuss the differences in primary diagnosis between children and adults with attention-deficit/hyperactivity disorder.
2. Describe how physician specialty and pharmacotherapy differ in treating children and adults with attention-deficit/hyperactivity disorder.

Summary:

Objective: This study examines the differences in outpatient treatment of attention-deficit/hyperactivity disorder in children and adults utilizing a national database.

Method: Data were analyzed in children (ages 5 ? 18) and adults (ages 19 and older) from a nationally representative survey of physicians using the National Ambulatory Medical Care Survey for years 1992 through 2002. Clinical characteristics, demographic data, and specialty of the treating physicians for both children (n=1666) and adults (n=670) with attention-deficit/hyperactivity disorder were compared.

Results: Over half of the children (56.5%) with attention-deficit/hyperactivity disorder were managed by primary care physicians, while the majority of adults (67.9%) were treated by psychiatrists. Comorbid psychiatric diagnoses were more common in adults than in children, and adults were more likely to be treated with anxiolytic and antidepressant medications. The use of psychostimulant medications was common in both groups of individuals.

Conclusion: Significant differences between the two age groups, including primary diagnoses, psychotropic medications utilized and treating physician specialties, were present and may contribute to the apparent disparity between children and adults being diagnosed and treated for attention-deficit/hyperactivity disorder.

References:

1. Wilens TE, Biederman J, Spencer TJ: Attention deficit/hyperactivity disorder across the lifespan. Ann Rev Med 2002; 53:113-131.
2. Faraone SV, Spencer TJ, Montano CB, Biederman J: Attention-deficit/hyperactivity disorder in adults. Arch Intern Med 2004; 164:1221-1226.
3. Bramble D: Psychostimulants and psychiatrists: the Trent adult psychiatry psychostimulant survey. J Psychopharm 2000; 14(1): 67-69.

NR1013

An Evaluation of Patient and Family Depression Monitoring

Carol A. Glod, Ph.D., *Northeastern University, Department of Nursing, 360 Huntington Avenue, 210 Robinson Boulevard, Boston, MA 02115,* Julie Totten, M.B.A.

Educational Objectives:

At the conclusion of this session, the participant should be able to assess the impact of a semi-structured depression monitoring kit on patients and their families.

Summary:

Objective: The purpose of this study was to assess whether adult depressed patients and their families benefit from reading and using a Depression Monitoring Kit for one month.

Method: This descriptive comparative study used online surveys to evaluate adult depressed patients and their families' knowledge of depression and current treatment status. Participants were recruited from the web site of Families for Depression Awareness (familyaware.org). One month following the receipt of a Depression Monitoring Kit, they were surveyed to evaluate their use of the kit, how much they learned, and their participation in treatment for depression.

Results: To date, 152 have participated, 92 persons with depression and 18 family members. Data collection continues. Preliminary findings indicate that more than half of respondents participated in both pharmacotherapy and psychotherapy (63%). Twenty-seven percent of the sample had been hospitalized psychiatrically, while 33% had been diagnosed with depression for 1-5 years, and 38% for over 5 years. Fifteen percent of family members reported using the Monitoring Kit once or twice a week. Of persons who used the Kit, 67% reported that it helped them learn at least a moderate amount about depression and its treatment, while 84% and 89%, respectively, reported learning much more about how families may help with treatment, and how to track and monitor depressive symptoms. Overall, 100% of participants reported that the Depression Monitoring Kit was helpful.

Conclusions: Persons with depression and their families report that participating in formal depression monitoring is helpful. The presence of a semi-structured monitoring kit can help promote effective treatment.

Funded in part by Families for Depression Awareness.

References:

1. Mann JJ. The medical management of depression. N Engl J Med. 2005 Oct 27;353 (17):1819-34.
2. Zahran HS, Kobau R, Moriarty DG, etc. Health-related quality of life surveillance?United States, 1993-2002. MMWR Surveill Summ. 2005 Oct 28;54(4):1-35.

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