Dissolving the Mind-Brain Barrier

Psychotherapy and Psychopharmacology:

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New York, NY • May 1-6, 2004
NR1  Monday, May 3, 9:00 a.m.-10:30 a.m.
Psychiatric and Substance-Use Disorders in an Advanced HIV Minority Cohort
Mubasher Naseer, M.A., Department of Pathology, Mount Sinai Medical Center, One Gustave Levy Place, New York, NY 10029-6574; Amy I. Tai, M.S., Jennifer G. Monzones, B.A., Elizabeth L. Ryan, Ph.D., Susan Morgello, M.D.
Educational Objectives:
At the conclusion of this session, the participants will have a greater understanding of the high prevalence of psychiatric and substance use disorders among this population. Concomitant diagnoses of substance use and mood disorders will be demonstrated. A need for greater vigilance to such pathology in diverse populations will be elucidated.
Summary:
Objective: While the prevalence of HIV has skyrocketed among minorities, research on the rates of psychiatric disorders among these individuals is scant.
Method: We report rates of disorders among an advanced HIV inner-city cohort (the Manhattan HIV Brain Bank) who were evaluated every six months via a semi-structured psychiatric interview (PRISM). The sample consisted of 209 patients (76% men) who were mostly minority (42% Black, 33% Hispanic).
Results: The most prevalent lifetime disorder was MDD (65%), with other diagnoses at much lower rates (i.e., Dysthymia: 16%, PTSD:15%, Mania: .09%). Similar patterns emerged for current psychiatric disorders, albeit at lower rates. Substance use disorders (SUDS) were comparable or exceeded psychiatric diagnoses. The most frequent lifetime dependence diagnoses were Cocaine (61%), Opiates (45%), Alcohol (43%), and Cannabis (19%). Rates for current dependence were high but lower than for lifetime. Urine toxicology results identified additional current substance users. Only 18% of the cohort was free of any SUD.
Conclusions: Rates of SUDS and psychiatric disorders are greater than those previously reported. Our results confirm the feasibility of using a semi-structured interview with an advanced HIV inner-city cohort and indicate exceedingly high rates of psychiatric disorders. Implications for treatment and psychiatric comorbidity will be discussed.
References:

NR2  Monday, May 3, 9:00 a.m.-10:30 a.m.
Dopaminergic Challenge in Adolescents With ADHD and Nicotine Dependence
Himanshu P. Upadhyaya, M.B., Psychiatry, Medical University of South Carolina, 1159 Sea Eagle Watch, Charleston, SC 29412; Wei Wang, M.D., Kathleen T. Brady, M.D.
Educational Objectives:
At the conclusion of this session, the participant should be able to learn about the involvement of dopaminergic system in adolescents with nicotine dependence.

NR3  Monday, May 3, 9:00 a.m.-10:30 a.m.
ADHD, Treatment, and Substance Use Pattern in College Students
Himanshu P. Upadhyaya, M.B., Psychiatry, Medical University of South Carolina, 1159 Sea Eagle Watch, Charleston, SC 29412; Kathleen O'Rourke, Ph.D., Kelly Rose, B.A., Wei Wang, M.D., Brian Sullivan, Psy.D., Kathleen T. Brady, M.D.
Educational Objectives:
At the conclusion of this session, the participant should be able to learn about substance use patterns among college students with ADHD.
Summary:
Introduction: The objective of this preliminary study was to examine ADHD treatment and substance use pattern among college students.
Methods: Three hundred and thirty four (334) older adolescents at a local college were surveyed about current ADHD symptoms and psychopharmacological treatment. The survey was conducted in conjunction with the annual CORE survey that explores the student's substance use patterns and attitudes.
Results: Participants with current ADHD symptoms were more likely to initiate cigarette smoking earlier (p=0.04), and have higher use of cigarettes (p=0.034) and “other” drugs (p=0.003) in the preceding year as compared to those without current ADHD symptoms. Participants on medication, with current ADHD symptoms, were more likely to use “other drugs” in the past month (p = 0.009) and tended to use more tobacco in the past year (p = 0.077) as compared to those without current ADHD symptoms. A significant minority of the participants reported abuse/diversion of their medication for recreational use.
Conclusion: Results of our preliminary study indicates that adequate symptom control for ADHD may be important to reduce substance use among college students with ADHD. Further pro-
spective studies in this population are warranted to examine the relationship between ADHD treatment, substance use, and medication abuse/diversion.

References:

NR4 Monday, May 3, 9:00 a.m.-10:30 a.m.
Ecstasy Use in the U.S. and Its Relationship With Other Drug Use and Dependence
Silvia S. Martins, M.D., Mental Health Department, Johns Hopkins School of Public Health, 624 N. Broadway, PO Box 671, Baltimore, MD 21205-1900; Guido Mazzotti, M.D., Howard D. Chilcoat, Sc.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize patterns of ecstasy users in USA and the association of ecstasy use with other drug use and dependence

Summary:
Background: Ecstasy use presents increasing trends in USA. Little is known about its natural history and its relationship with other drugs abuse.

Objectives: To compare chronic versus new ecstasy users and marijuana users by lifetime drug use and dependence.

Method: Secondary analysis from the 2001 National Household Survey on Drug Abuse (n= 5,561 respondents). Data were matched using binary logistic regression models performed with STATA 8.0.

Results: Prevalence of ecstasy use was higher for males and whites. Marijuana use typically preceded ecstasy use which preceded cocaine/heroin use. Chronic ecstasy users were more likely to use cocaine, crack, heroin, LSD, inhalants, tranquilizers, stimulants and sedatives (ORs=3.97); be alcohol dependent (OR=3.27), cocaine dependent (OR=4.78) and heroin dependent (OR=5.93) compared to new users. Ecstasy users were more likely to use cocaine, inhalants, tranquilizers and stimulants versus marijuana users (ORs=1.44). Chronic ecstasy users were more likely to be cocaine dependent (OR=1.73) and heroin dependent (OR=2.15) than marijuana users.

Conclusion: Chronic ecstasy users have higher occurrence of other drug use and dependence than recent onset ecstasy users and marijuana users. These findings suggest early intervention for ecstasy users can potentially attenuate the progression to multiple use or dependence of drugs.

References:

NR5 Monday, May 3, 9:00 a.m.-10:30 a.m.
Bipolar Disorder, Substance Abuse, and Antidepressant-Induced Mania
Sumita G. Manwani, M.D., Psychiatry Department, Cambridge Hospital, 1493 Cambridge Street, Cambridge, MA 02139, Tamara B. Pardo, B.A., S. Nassir Ghaemi, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to study whether substance use disorders are a potential risk factor for antidepressant induced mania in bipolar patients.

Summary:
Objective: Substance use disorder (SUD) has been associated with increased risk for antidepressant-induced mania (ADM) in bipolar disorder (1). This analysis seeks to confirm these findings, and identify other predictors of ADM (2).

Method: In a partial data analysis, we examined 108 trials in 30 bipolar disorder patients involving SUD (n=65) and no SUD (n=43). The full data analysis of about 400 trials will be presented.

Results: Crude rates demonstrated no notable difference in risk of ADM in SUD patients (19.3%) vs. non-SUD patients (25.6%) (p=0.71). Adjusted for potential confounders (age, gender, type of substance, number years ill, number of MDEs, number manic/hypomanic episodes, number AD trials total, and type of AD), logistic regression again reveals no notable impact of SUD for ADM risk (OR=1.37, [0.04, 47.2]). History of >10 past manic/hypomanic episodes was the main ADM predictor (OR=15.2, [1.03, 224.7]; 29.8% in high manic/hypomanic episode group vs. 11.9% in low episode group). Interestingly, among specific substances, the main observation was decreased ADM risk with cocaine abuse (OR=0.008, [0.0001, 0.48]; 7.7% in cocaine abusers vs. 24.1% in non-abusers).

Conclusions: SUD may not increase risk of ADM, but >10 past manic/hypomanic episodes may be a major ADM predictor.

References:
2. Henry C, Sorbara F, Lacoste J, Gindre C, Leboyer M. Antidepressant-induced mania in high manic/hypomanic episode group vs. low episode group. Interestingly, among specific substances, the main observation was decreased ADM risk with cocaine abuse (OR=0.008, [0.0001, 0.48]; 7.7% in cocaine abusers vs. 24.1% in non-abusers).

NR6 Monday, May 3, 9:00 a.m.-10:30 a.m.
Defense Mechanisms in Patients With Panic Disorders Before and After Cognitive-Behavioral Therapy
Gisele G. Manfro, M.D., Department of Psychiatry, HCPA, Luiz Manoel Gonzaga 630/11, Porto Alegre, RS 90470-280, Brazil; Carolina Blaya, M.D., Elizeth Heldt, Leticia Kipper, Luciano Isolan

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize that panic disordered patients use maladaptive defense mechanisms according to DSO-40 and that these patients use less neurotic defense mechanisms after achieving remission with CBT.

Summary:
Defense mechanisms are used to evaluate psychodynamic functioning and are an important dimension of the structure of personality. Studies have demonstrated that patients with panic disorder (PD) use a more maladaptive pattern of defense mechanisms, but there is little data involving the study of the use of these mechanisms during the symptomatic stage and after PD
remission. The aim of this study is to evaluate the defense mechanisms used by patients with PD refractory to medication treatment and to verify whether the use of these mechanisms modify with the augmentation of cognitive-behavioral therapy.

Methods: Twenty-nine panic disordered patients, according to the DSM-IV criteria, participated in the study. The M.I.N.I. was used to perform the diagnostic evaluation of patients. The severity of the panic disorder was evaluated by the C.G.I. and by the Panic Inventory. The defense mechanisms were evaluated by the DSQ-40 (Defense Style Questionnaire). The instruments were applied at the baseline and after 12 session cognitive-behavioral group therapy.

Results: Patients decrease the use of neurotic defenses (5.1 vs. 4.7, p=0.04) and there is a trend to decrease immature defenses (4.6 vs. 4.2, p=0.07) with CBT. Remission (CGI ≤ 2 and no attacks) influences the differences in the use of neurotic mechanisms (p=0.04).

Conclusion: Panic disordered patients use less maladaptive defenses after achieving remission with CBT.

References:

NR7 Monday, May 3, 9:00 a.m.-10:30 a.m.
Comorbidity of Anxiety Disorders in a Community Setting
Matthew G. Biel, M.D., Psychiatry Department, New York University, 214 Mulberry Street, Apt. 6E, New York, NY 10012; Brady G.S. Case, M.D., Eric D. Peselow, M.D., Mary Anne Pressman, M.D., Mary T. Guardino, B.A.

Educational Objectives:
At the conclusion of this session, the participant should be able to understand the frequency of comorbidity among the various anxiety disorders and depression so we can get a better understanding of treating these disorders.

Summary:
Objective: The purpose of this paper is to evaluate the comorbidity of all of the anxiety disorders with other anxiety disorders (OCD, social & specific phobias, generalized anxiety disorder) & depression, in order to assess frequency of comorbid diagnosis. Method: Over the past 10 years, at the Freedom from Fear Clinic in Staten Island N.Y. (an outpatient anxiety disorder clinic associated with Columbia University) we have evaluated 706 patients who were primarily diagnosed with either panic disorder, OCD, social phobia, generalized anxiety disorder or depression using a modified symptom check list adapted from the SCID during the acute stage of the illness. Results: Overall only 63 of the 213 patients (29.6%) of the sample met criteria for a single diagnosis (one of the four other anxiety disorders or depression). 142 of the 213 patients met criteria for panic with agoraphobia (66.7%). Comorbidity of panic was as follows: Panic with other anxiety disorders or depression 196/255 (76.9%); Depression with other anxiety disorders 192/281 (68.2%); Social phobia other anxiety disorders or depression 28/48 (58.3%); OCD other anxiety disorders or depression 57/90 (63.3%); GAD other anxiety disorders or depression 27/32 (84.4%). Conclusions: Overall the diagnosis of anxiety disorders was associated with a high rate of comorbidity. The greater the number of anxiety diagnoses the poorer the response to treatment of the panic disorder. Implications of these findings will be discussed.

References:

NR8 Monday, May 3, 9:00 a.m.-10:30 a.m.
GAD in General Practice in the Nordic Countries: Conspicuous and Hidden
Supported by Wyeth Pharmaceuticals
Povi Munk-Joergensen, Aalborg Psychiatric Hospital, Mølleparkvej 10, Aalborg, DK 9000, Denmark, Ib Rasmussen, M.D., Christer Allgulander, M.D., Alv A. Dahl, M.D., Anti Virta, Martin Holm, Leslie Folager

Summary:
Approximately 50% of the frequent disorders such as depression, anxiety, and somatisation remain unrecognized to the general practitioner. The purpose of the study is to estimate the prevalence of GAD in general practices in the Nordic countries (Denmark, Finland, Norway, and Sweden), determine the rate conspicuous/hidden and identify predictors for recognition. 656 general practitioners (GP) from the four Nordic countries participated in the study. GP filled in a schedule characterizing the practice and the doctor, the patient filled in a questionnaire about symptomatology, depression, and other studies Generalized Anxiety Screening Questionnaire (GAS-Q), and depression, Depression Screening Questionnaire (DSQ) making it possible to diagnose GAD and other anxiety disorders, and major depression according to DSM IV criteria. The general practitioner filled in a schedule Generalized anxiety and Depression in Primary care (GAD-P) giving his/her statement about patients mental disorders (if any) not knowing the result of the patients schedule. 8879 patients participated in the study, 471 were identified as meeting the full GAD criteria. Overall GAD prevalence was 5.6% (4.7% - 6.4%). Identification rate was overall 37.9% (range 33.8% - 53.2%). Important predictors for identification were: Patient subjective feeling of anxiety, depression, impairment by psychological problems and worries unable to handle. Predictors are analysed in a multi variant statistical model. Identification of GAD in general practice may be improved by focusing on Patient subjective feeling of anxiety, depression, impairment by psychological problems and worries unable to handle.

NR9 Monday, May 3, 9:00 a.m.-10:30 a.m.
State-Trait Anxiety and Anxiety Sensitivity in Predicting 35% Carbon Dioxide Response
Emel S. Monkul, M.D., Department of Psychiatry, UTHSCSA, 7703 Floyd Curl Drive, San Antonio, TX 78229; John P. Hatch, Ph.D., Elif Onur, M.D., Tunc Akin, M.D., Umit Tural, M.D., Huray Fidaner, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the difference between anxiety sensitivity and state
and trait anxiety, and the effects of these on the response to 35% CO₂ challenge.

Summary:

Objective: The aim of this study was to examine the effects of state-trait anxiety and anxiety sensitivity on response to a CO₂ challenge in panic disorder patients (PD), their healthy first-degree relatives (HR) and healthy controls (HC).

Methods: Our sample consisted of 32 DSM-IV PD, 32 HR and 34 HC. We used air (placebo) and a mixture of 35%CO₂/65%O₂. Anxiety Sensitivity Index (ASI) and State-Trait Anxiety Inventory for subjective anxiety and Panic Symptom List for panic symptoms were used. A CO₂-induced panic attack was defined by an increase from baseline >1 points in at least 4 panic symptoms, at least one being a cognitive symptom.

Results: PD had increased anxiety sensitivity and state-trait anxiety scores compared to HR and HC (ANOVA, p<0.001); the difference between HR and HC was not significant. A past history of suffocation increased the risk of CO₂ reactivity (Odds ratio=3.13, CI=1.19-8.20) in the whole group. In female PD high ASI and trait anxiety predicted CO₂-induced panic (logistic regression analysis, p<0.05).

Conclusions: ASI seems to have a gender-specific relation to CO₂ reactivity. History of suffocation might be an important predictor of CO₂-induced panic. This work was partly supported by an award from Turkish Psychiatric Association, Izmir Branch.

References:
1. van Beek N, Griez E: Anxiety sensitivity in first-degree relatives (HR) and healthy controls (HC). Biol Psychiatry 2000; 47:830-835.

NR10 Monday, May 3, 9:00 a.m.-10:30 a.m.
Changes in Biofeedback Variables After Pharmacotherapy in Panic Disorder
Bum-Hee Yu, M.D., Department of Psychiatry, Samsung Medical Center, 50 Iwon-Dong, Gangnam-Gu, Seoul 135-370, Korea; Moon S. Koo, M.A.

Educational Objectives:
At the conclusion of this session, the participant should be able to understand the relationship between anxiety and biofeedback variables in panic disorder understand the availability of EDR as a sensitive index to reflect treatment response in panic disorder.

Summary:

Objective: Anxiety has been known to be related with some pathophysiologic variables. This study aimed to find the changes in the biofeedback variables after pharmacotherapy.

Method: We recruited 38 panic patients (M:25 F:13, according to the DSM-IV) at the Samsung Medical Center in Seoul and 33 normal control subjects (M:21 F:12). Panic patients were treated with paroxetine. All subjects were assessed both at the beginning of the study and 3 months after pharmacotherapy. We measured forearm EMG, frontal EMG, electrodermal response (EDR), and body temperature using the Procomp & Biograph biofeedback instrument. Hamilton Anxiety Rating Scale (HAM-A), Hamilton Depression Rating Scale (HAM-D), Beck Depression Inventory (BDI), Spielberger State and Trait Anxiety Inventory (STAI-S, STAI-T) and Acute Panic Inventory/API were also measured.

Result: Panic patients showed higher baseline EDR (p=0.033), compared with normal control subjects. Panic patients showed higher scores on HAM-A, HAM-D, BDI, STAI-S, STAI-T, and ASI (all p values<0.001). After 3 months of pharmacotherapy, panic patients improved on baseline EDR (p=0.016), stress EDR (p=0.021), and recovery EDR (p=0.004), and showed significant improvement in HAM-A, HAM-D, BDI, STAI-S, STAI-T, ASI, and API. (all p-values <0.001)

Conclusions: EDR measured by the biofeedback instrument decreased after pharmacotherapy in panic disorder. Thus, EDR may be a sensitive index to reflect treatment response in panic disorder.

References:

NR11 Monday, May 3, 9:00 a.m.-10:30 a.m.
An Efficacy Comparison of Atypical Antipsychotic Medications for PTSD
Naomi M. Mendelovicz, M.D., Psychiatry Department, Dartmouth Medical School, One Medical Center Drive, Lebanon, NH 03756; Bradley V. Watts, M.D., David H. Rubin, M.D., Rebecca L. Hirsch, M.D., Keith R. Warren, M.D., Bradley A. McLure, M.D., Lorna K. Mayo, M.D.

Educational Objectives:
At the conclusion of this presentation, the participants should demonstrate an understanding about the comparative efficacy of atypical antipsychotic medications for posttraumatic stress disorder.

Summary:

Objective: There is accumulating evidence regarding the use of atypical antipsychotic medications for treatment of post-traumatic stress disorder (PTSD). There are no trials that compare the efficacy of these agents. This project seeks to compare the efficacy of atypical antipsychotic agents in treatment of PTSD.

Method: A retrospective chart review was performed on 982 patients diagnosed with PTSD treated in the outpatient mental health clinic at the White River Junction VA Medical Center in 2001. The global assessment of function scores (GAF) for patients starting treatment with an atypical antipsychotic medication was obtained.

Results: Nineteen percent of patients with PTSD in the outpatient clinic received an atypical trial during 2001. Of those, 54% were treated with quetiapine, 26% with olanzapine, and 19% with risperidone. The average change in GAF score was 4.9 for quetiapine, 4.6 for olanzapine, and 3 for risperidone. Each agent showed statically significant change in mean GAF from baseline. There was no significant difference in the mean change or percent of patients improved between any agents.

Conclusions: Atypical antipsychotic agents were commonly used in this patient population to treat PTSD. Each medication showed statistically significant improvement in GAF scores. There was no significant difference in the efficacy comparing agents.

References:
NR12  Monday, May 3, 9:00 a.m.-10:30 a.m.
Skin Picking: A Symptom Across Multiple Diagnoses
Dena C. Rabinowitz, Ph.D., Bio-Behavioral Institute, 935
Northern Boulevard, Suite 102, Great Neck, NY 11021; Fugen
Neziroglu, Ph.D., Matthew Jacobson, M.A., Anna Breytman,
Ph.D., Jose A. Yaryura-Tobias, M.D.
Educational Objectives:
At the conclusion of this session, the participant should be able
to recognize skin picking due to increased awareness of related
behaviors and emotions linked to this symptom. Participants
should also be able to identify important aspects of skin picking
behavior as it is related to different psychiatric diagnoses and
treatment.
Summary:
Objective: Although skin picking behavior is observed in numer-
ous diagnostic entities such as Body Dysmorphic Disorder, Obses-
sive-Compulsive Disorder, Trichotillomania, and Borderline Per-
sonty Disorder, it has received relatively little attention in the
psychological literature. The current study sought to examine de-
scriptive details about skin picking behavior.
Method: Thirty participants who reported that they engage in
skin picking completed self-report questionnaires assessing demo-
graphic, symptom, and diagnostic information.
Results: Participants ranged from ages 19-77 and 70% of partic-
ips were women. Overall, participants reported that they experi-
cenced negative feelings prior to picking such as anxiety, loss
of control, tension, and general negative mood. After picking,
participants did not report a substantial reduction in these emo-
tions but an increase in intensity and types of negative mood states
including shame, guilt, and physical pain. Information regarding
location, triggers, and implements for picking, frequency, duration
level of interference was also gathered.
Conclusion: The findings offer new information about skin pick-
ning behavior and offer a behavioral analysis of this often neglected
symptom. Implications for diagnosis, treatment, and relevance in
Body Dysmorphic Disorder are also addressed.

References:
1. Neziroglu F, Mancebo M. Skin picking as a form of self injurious
2. Yaryura-Tobias JA, Mancebo M, Neziroglu F. Clinical and theo-
retical issues in self injurious behavior. Rev Bras Psiquiatr

NR13  Monday, May 3, 9:00 a.m.-10:30 a.m.
ADHD Comorbidity and Gender Differences in
Children
Anela Bolfek, M.D., Psychiatry Department, Tufts - NEMC, 750
Washington Street, 1007, Boston, MA 02111; Atilla Turgay,
M.D., Rubaba Ansari, M.A., David Ng, M.D.
Educational Objectives:
At the conclusion of this session, insight into the nature and
frequency of comorbid disorders in ADHD - differentiate gender
differences in ADHD comorbidities
Summary:
Objective: Most attention-deficit/hyperactivity disorder (ADHD)
studies are based on small samples, which do not provide reliable
information on gender differences and comorbidities in specific
age groups. This study with 1655 patients provided more reliable
information.
Methods: The patients were diagnosed according to DSM-IV
criteria, DuPaul ADHD Rating Scale, and Offord-Boyle Child
Health Study parent and teacher rating scales.
Sample: The patient sample consisted of 1318 (79.64%) males
and 337 (20.36%) females, 6-12 years of age. They were seen in
a university hospital, ADHD clinic, training and research institute.
Results: Most patients (77.89%) suffered from two or more
disorders. Oppositional Defiant Disorder, Conduct Disorder, and
Anxiety Disorders were most common (60.36%, 19.27%, 11.30%
respectively). Also observed were Dysmorphic Disorder, Pervasive
Developmental Disorders, and Major Depression (4.05%, 3.50%,
2.30% respectively). A greater number of males were observed in
any given comorbidity (ratios ranged from 3.2:1 to 5.5:1). However,
females were more likely to have comorbid Anxiety Disorders or
Dysmorphic Disorder than males (13.35% vs. 10.77%, 5.04% vs.
3.79% respectively).
Conclusion: It is highly likely that an ADHD patient will develop
other disorders. ADHD patients should be carefully screened for
other comorbidities, for which additional medications may be re-
quired.

References:
peractivity disorder subtypes and comorbid disruptive disor-
ders in a child and adolescent mental health clinic. Can J
Psychiatry 43:623-628
Tic disorder in children and adolescents with ADHD. Abstract in
print for Pediatric Child Health, the Canadian Pediatric Society
Journal, June issue
Comorbidities in conduct disorder may determine the type of
medication treatment. Abstract in print for Pediatric Child
Health, the Canadian Pediatric Society Journal, June issue

NR14  Monday, May 3, 9:00 a.m.-10:30 a.m.
Suicidality in Depressed Patients With and Without a
History of Alcoholism
Leo Sher, M.D., Department of Psychiatry, Columbia University,
1051 Riverside Drive, Suite 2917, Box 42, New York, NY
10032; Maria A. Oquendo, M.D., Hanga G. Galfalvy, Ph.D.,
Michael F. Grunebaum, M.D., Ainsley K. Burke, Ph.D., J. John
Mann, M.D.
Educational Objectives:
At the conclusion of this session, participants should be able
to identify risk factors for suicidal behavior in depressed patients
with a history of alcoholism.
Summary:
Introduction: Studies suggest that depressed subjects with a
history of alcoholism have more chronic impairment and higher
suicidality than individuals with either diagnosis alone. We hypo-
thesized that smoking and aggression contribute to higher suicidality
in depressed subjects with a history of alcoholism compared to
depressed subjects without a history of alcoholism.
Methods: Two hundred nineteen depressed subjects without a
history of any alcohol or substance abuse/dependence and 129
depressed individuals with a history of alcohol abuse/dependence
participated in the study. All subjects were free from alcohol or
substance abuse for at least 2 months. Demographic and clinical
parameters were assessed and recorded.
Results: The logistic regression analysis indicates that higher
prevalence of suicide attempters in the group with a history of alcoholism
is related to higher aggression scores in the former group. Higher
suicide ideation scale scores in depressed subjects with a history
of alcoholism is related to higher prevalence of smoking and higher
aggression scores in this group compared to the other group.
Conclusions: Our findings suggest that in addition to obtaining a history of depression and suicidal behavior, clinicians should assess comorbidity with alcoholism and cigarette smoking, and personality features such as aggression.

References:


NR15  Monday, May 3, 9:00 a.m.-10:30 a.m.
QEEG and P300 in Patients With Hepatoencephalopathy

Sang-Ick Han, M.D., Department of Neuropsychiatry, Out Lady of Mercy Hospital, 665 Pupyung-Dong, Pupyung-Gu, Inchon 403-720, South Korea; Wan-Seok Yang, M.D., Yang-Whan Jeon, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize that the alpha band analysis of quantitative electroencephalogram and auditory and visual P300 could be useful for exploring the cognitive dysfunctions in patients with hepatic encephalopathy.

Summary:

Objective: Digitalized quantitative electroencephalogram (QEEG) and P300 event-related potentials (ERP) were used to detect mild cognitive dysfunctions at the early phase in patients with hepatic encephalopathy.

Method: Digitalized QEEG and auditory and visual “oddball” paradigm P300 were employed in normal controls (N=12) and patients with brain concussion (N=6). EEG activity was recorded from 25 electrodes, referred to nose. Auditory stimulus categories were defined as the standard (1000 Hz, 80%) and target (2000 Hz, 20%) with the intensity of 75dB. Visual stimulus categories were defined as the standard (circle, 3.5 cm diameter, 80%) and target (square, 15 cm on a side, 20%). The stimuli were presented in random series, once every 2 seconds.

Results: The dominant alpha was smaller and lower in patients with hepatic encephalopathy in occipital areas (F=10.7, P<0.01). P300 was delayed (F=16.8, P<0.01) and smaller (F=17.1, P<0.01) across both auditory and visual modalities in patients with hepatic encephalopathy. Visual P300 was more delayed than auditory P300 in patients with hepatic encephalopathy (F=12.4, P<0.01), but not smaller (F=1.9, n.s.).

Conclusions: QEEG and P300 ERPs, especially visual P300 latency, could be used as an early detector for mild brain dysfunctions in patients with hepatic encephalopathy.

References:


NR16  Monday, May 3, 9:00 a.m.-10:30 a.m.
P300 in Patients With Brain Concussion

Sang-Ick Han, M.D., Department of Neuropsychiatry, Out Lady of Mercy Hospital, 665 Pupyung-Dong, Pupyung-Gu, Inchon 403-720, South Korea; Wan-Seok Yang, M.D., Yang-Whan Jeon, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize that P300 could be useful for exploring cognitive dysfunctions in patients with brain concussion.

Summary:

Objective: Although abnormal MRI findings were not shown in patients with brain concussion by traffic accidents, it has been well known that their cognitive dysfunctions could be complained. This study was design to examine the availability of P300 as an objective measure reflecting minor brain dysfunctions.

Method: Auditory and visual “oddball” paradigms were employed in normal controls (N=12) and patients with brain concussion without MRI abnormalities (N=12). Auditory stimulus categories were defined as the standard (1000 Hz, 80%) and target (2000 Hz, 20%) with the intensity of 75dB. Visual stimulus categories were defined as the standard (circle, 3.5 cm diameter, 80%) and target (square, 15 cm on a side, 20%). The stimuli were presented in random series, once every 2 seconds.

Results: P300 in patients with brain concussion was elicited later (F=14.4, P<0.001) and smaller (F=45.8, P<0.0001) across the both auditory and visual modalities. There were no interactions groups (controls vs. patients) and modalities (auditory vs. visual) in P300 latency (F=0.2, n.s.) and in P300 amplitude (F=0.3, n.s.).

Conclusions: Even though brain lesion was not shown by MRI in patients with brain concussion, the subtle cognitive dysfunctions could be detected by both auditory and visual P300.

References:


2. Sangal RB, Sangal JM: Closed head injury patients with mild cognitive complaints without neurological or psychiatric findings have abnormal visual P300 latencies. Biol Psychiatry 1996; 38:305-307

NR17  Monday, May 3, 9:00 a.m.-10:30 a.m.
One ECT Session Is Not Sufficient to Produce Memory Dysfunction: A Controlled Study

Lorena Rami-Gonzalez, Ph.D., Department of Psychiatry, Hospital Clinic, Villarreal, Barcelona, Spain; Javier Goli, Teodor Marcos, Ph.D., Miguel Bernardo, M.D., Maria J. Portella, M.S.C., Manel Salamero, M.D.

Educational Objectives:

At the conclusion of this session, the absence of memory impairment after one M-ECT session reinforce the efficiency of this treatment and would perhaps facilitate the inclusion of patients in M-ECT programs.

Summary:

Background: Memory dysfunction is one of the main adverse effects of ECT treatment. Information consolidation and retrieval depend on the medial temporal lobe and on hippocampal-diencephalic functional circuits. These areas are the most predisposed to unchain massively Long Term Potentiation (LTP) neuronal plasticity phenomenon. The massive LTP induction has been pro-
posed as a neurophysiological bases of the memory disorders by ECT.

Aim: To know if one ECT session may be sufficient to unchain neurophysiological mechanisms to produce significant memory impairment.

Method: Twenty-four psychiatric outpatients treated with M-ECT. Twelve patients were assessed before and nineteen minutes after an ECT session. Twelve patients treated with M-ECT were used as control group and were assessed when they arrived at the hospital and nineteen minutes after, just before ECT session.

Results: Experimental group do not show a marked shift in cognitive functions in the second test session. Groups only differed significantly in visuospatial test F (1, 18) = 7.04, P = 0.015.

Conclusions: One M-ECT session may not permit massive LTP and NMDA receptors dysfunction to produce memory or other cognitive dysfunction. Otherwise, we found a visuospatial dysfunction, suggesting that one ECT may implicate an asymmetrical transitory dysfunction on right hemispheric.

References:

NR18 Monday, May 3, 9:00 a.m.-10:30 a.m.
Tau-Protein and Beta-Amyloid as Diagnostic Markers of Alzheimer’s Dementia
Vladimir Pidrman, M.D., Psychiatry Department, University Hospital, I.P. Pavlova 12, Olomouc, CZ 77520, Czech Republic; Klara Latalova, Jiri Mares, M.D., Karel Urbanek, M.D.

Educational Objectives:
At the conclusion of this session, the examinations of tau-protein and beta-amyloid levels (in cerebrospinal liquor) may be suitable for diagnostic Alzheimers dementia and eliminating vascular dementia.

Summary:
Assumption: Changes levels of tau protein (increasing) and beta-amyloid (decreasing) are suitable marker for early AD diagnosis. The levels of tau protein and beta-amyloid in liquor were examined in a group of 21 patients with multiple sclerosis. Additionally, in patients with dementia genotyping of apolipoprotein E was carried out and the biochemical and genetic results of the measurements were compared with clinical findings.

Tau protein levels in liquor were increased in 67 % of patients with AD, in 7 % in patients with vascular dementia (VD) and 17% in patients with mixed dementia (MD). Beta-amyloid levels were decreased in 67 % of AD, 33 % of VD and 33 % of MD. Contemporarily tau protein increasing and beta-amyloid decreasing was in 50 % of AD, 22 % of VD and 0 % of MD. In control set of patients with multiple sclerosis tau protein levels were increased in any case (in opposite level was decreased in 71 %); beta-amyloid decreasing was in 81 % cases. On base evaluating of tau protein and beta-amyloid proportions was possible confirm clinical diagnosis of AD surely in 50 % cases, borderline in 33 % cases.

References:

NR19 Monday, May 3, 9:00 a.m.-10:30 a.m.
Predictors of Eating Disorder: Symptoms Across Ethnic Groups
Marney A. White, Ph.D., Psychiatry Department, Yale University, 301 Cedar Street, Second Floor, New Haven, CT 06519; Carlos M. Grilo, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to understand different components of eating and body image disturbances in adolescent girls and understand the predictors of these symptoms across ethnic groups.

Summary:
Objective: To examine ethnicity patterns in eating and body image disturbances in psychiatrically hospitalized female adolescents.

Method: Subjects were 427 (54 African American, 320 Caucasian, 53 Latina) inpatients. Ethnic groups were compared on measures of dietary restraint, body image, binge eating, and purging. Psychological measures (depression, anxiety, impulsivity, self-devaluation, peer insecurity, child abuse) were examined as predictors of these eating and body image disturbances separately for the ethnic groups.

Results: Caucasians reported significantly higher levels of body image disturbance and dietary restraint than African Americans and Latinas (p < .001); binge eating and purging did not differ by ethnicity. Regression analyses indicated that for Caucasian and Latina girls, body image (43.8%, 47.1% of the variance) was explained by self-devaluation. For African Americans, body image (63% of the variance) was explained by self-devaluation, peer insecurity, and anxiety. For Caucasians, dietary restraint (34.8% of the variance) was explained by body image, depression, peer insecurity, and child abuse. For Latinas, restraint (32.9% of the variance) was explained by body image disturbance in college and impulsivity, whereas for African American girls, only body image disturbance predicted restraint (29.7% of the variance).

Conclusions: These findings indicate that different factors may contribute to the development of eating and body image psychopathology across ethnic groups. Findings raise questions regarding aspects of existing models of eating disorders for minority girls.

References:

NR20 Monday, May 3, 9:00 a.m.-10:30 a.m.
Body Dissatisfaction After Weight Restoration in Anorexia Nervosa
Joanna E. Steinglass, M.D., Department of Psychiatry, New York State Psychiatric Institute, 1051 Riverside Drive, Unit 98, New York, NY 10032; Laurel Mayer, M.D., B. Timothy Walsh, M.D.
Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the complexity of body image disturbance in anorexia nervosa and appreciate that the course of psychological improvement may be distinct from physical improvement.

Summary:
Objective: This study aimed to assess change in body image in women with anorexia nervosa (AN) by assessing body dissatisfaction (BD) with weight normalization, as compared to controls.
Method: Subjects were 17 women hospitalized for AN, and 7 normal controls. BD was measured before and after weight gain and after 6 months of weight maintenance, using the Eating Disorder Inventory-Body Dissatisfaction subscale (EDI-BD) and the Color-A-Person Test (CAPT). The CAPT provides a measure of the affective component of body image. Subjects also completed standard psychological measures.
Results: At low weight, patients had significantly higher scores on both measures of BD compared to controls. After weight restoration, there was no significant change in BD scores, despite significant improvement in depression and anxiety. Data collection is ongoing, but preliminary analysis of the follow-up data (N=5) shows significant improvement on the CAPT.
Conclusions: BD neither worsens nor improves with weight normalization in hospitalized women undergoing treatment for AN. There may be significant improvement in BD with weight maintenance.

References:

NR21
Monday, May 3, 9:00 a.m.-10:30 a.m.
Appearance Versus Health Reasons Among Obese Patients With Binge-Eating Disorder
Deborah L. Reas, Ph.D., Psychiatry Department, Yale School of Medicine, 301 Cedar Street, PO Box 208098, New Haven, CT 06520-8098; Carlos M. Grilo, Ph.D., Robin M. Masheb, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to understand the importance of assessing reasons for treatment seeking among obese patients with binge eating disorder and recognize the clinical implications of treatment seeking due to appearance concerns.

Summary:
Objective: This study examined reasons for seeking treatment reported by obese men and women diagnosed with binge eating disorder (BED).
Method: Participants were 248 consecutive treatment-seeking obese adults (58 men and 190 women) who met DSM-IV criteria for BED, based on semi-structured diagnostic interviews. Patients' reasons for seeking treatment were examined with respect to demographic (gender and age), obesity (BMI and age of onset), features of eating disorders, and associated psychological functioning (depression and self-esteem).
Results: Of the 248 participants, 64% reported health concerns and 36% reported appearance concerns as their primary reason for seeking treatment. Reported reasons for seeking treatment did not differ significantly by gender. Patients seeking treatment due to appearance-related reasons had significantly lower BMIs than those reporting health-related reasons (BMI = 34.8 versus 38.5, respectively; p<.001), but reported significantly greater body dissatisfaction (p<.001), significantly more features of eating disorders (p<.05), and lower self-esteem (p=.02).
Conclusions: Reasons that prompt treatment seeking among obese individuals with binge eating disorder warrant assessment and consideration during treatment planning, as they reflect meaningful patient characteristics.

References:

NR22
Monday, May 3, 9:00 a.m.-10:30 a.m.
Clinic Bias in Binge-Eating Disorder Exists for Black Women
Christine Lozano-Blanco, Ph.D., Psychiatry Department, Yale School of Medicine, 301 Cedar Street, New Haven, CT 06519; Robin M. Masheb, Ph.D., Carlos M. Grilo, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to diagnose binge eating disorder and recognize differences in clinical characteristics of black and white women who seek or do not seek treatment.

Summary:
Objective: To investigate sampling bias as it affects recruited clinic samples of black and white women with binge eating disorder (BED).
Methods: Clinical characteristics of a recruited clinic sample (220 consecutive BED cases) were compared with a community sample. Comparisons were performed separately for black and white women. Clinic and community groups were assessed with identical methods, including diagnostic interviews and established measures of features of eating disorders.
Results: In the clinic group, black and white women did not differ significantly in binge eating or eating-related psychopathology, but black women had significantly higher body mass index (BMI) than white women (p<.005; effect size = .75), substantially higher eating-related psychopathology (effect sizes ranged .48 to 1.25), but reported lower frequencies of binge eating than the community sample (effect size = -.57).
Conclusions: Our findings suggest that there does not appear to be a sampling bias among recruited clinic samples of white women with BED. A sampling bias appears to exist among clinic samples of black women with BED.

References:
NR23  Monday, May 3, 9:00 a.m.-10:30 a.m.  
A Controlled Comparison of Standard and Appetite-Focused Cognitive-Behavior Therapy for Binge-Eating Disorder  
Supported by National Institutes of Health  
Katherine A. Elder, Ph.D., Psychiatry Department, Yale University, 245 N. Main Street, Apt. 4, Wallingford, CT 06492; Linda W. Craighhead, Ph.D., Arnica L. Buckner, M.A., Heather M. Niemeier, M.A., Meredith A. Dung, M.A.  
Educational Objectives:  
At the conclusion of this session, the participant should be able to: 1) understand the rationale and techniques used in an appetite-based CBT treatment of binge eating disorder; 2) identify the key differences between standard and appetite-focused CBT; and 3) understand the efficacy of both treatments used as early interventions in a college-aged population.  
Summary:  
Objective: To compare the efficacy of two early intervention group treatments for binge eating disorder (BED): Cognitive-behavioral therapy (CBT) and a modified version of CBT, appetite-focused CBT (CBT-AF)  
Method: Twenty overweight college-aged women with subclinical or recent-onset BED were assigned to one of the two conditions and participated in 10 weekly sessions. Outcome was assessed at 1 and 4 months posttreatment.  
Results: Overall, participants in the CBT and the CBT-AF treatment groups demonstrated substantial, but not differential, improvement in eating disorder psychopathology and general psychiatric distress. Participants reported significant change in the following areas: decrease in number of objective binge episodes ($p < .001$, partial $\eta^2 = .53$) and reduction in eating disorder symptomatology (on the EDE-Q, $p < .001$, partial $\eta^2 = .53$), as well as improvement in body image, and decline in general psychopathology. These gains were evident at 1- and 4-months posttreatment.  
Conclusions: The results support the efficacy of both CBT-based early interventions for BED, and demonstrate that such treatments can be successfully delivered in a brief group format. Appetite monitoring may be a viable alternative to monitoring food intake within CBT in a subclinical or recent-onset population with BED.  
References:  

NR24  Monday, May 3, 9:00 a.m.-10:30 a.m.  
Childhood Abuse and Cluster "B" Comorbidity in Bipolar Disorder  
Jessica L. Garmo, Ph.D., Department of Psychology, Long Island University, 6 Silvermine Drive, South Salem, NY 10590; Joseph F. Goldberg, M.D., Paul M. Ramirez, Ph.D., Barry A. Ritzler, Ph.D.  
Educational Objectives:  
At the conclusion of this session, the participant should be able to familiarize participants with the phenomenology, prevalence, and clinical impact of childhood abuse, personality disorder comorbidity and their correlates in patients with bipolar disorder.  
Summary:  
Background: Phenomenologic overlap between bipolar disorder and borderline personality disorder has engendered ongoing debate about their nosologic distinctions and respective treatment outcomes. Childhood trauma has been implicated in the pathogenesis and self-destructive behaviors of borderline personality disorder, but less empirical study has addressed these features in bipolar illness, or their prevalence when both disorders co-occur.  
Method: One hundred DSM-IV bipolar I and II patients underwent SCID I and II diagnoses to ascertain comorbid cluster "B" personality features. Lifetime suicide attempts, substance abuse, and related components of course and outcome were examined relative to Axis II comorbidity and childhood abuse.  
Results: Thirty percent of bipolar subjects met DSM-IV criteria for cluster "B" personality disorders, which in turn were linked with histories of childhood emotional or physical abuse and emotional neglect, as well as more extensive substance abuse and lifetime suicide attempts. Logistic regression analysis indicated that suicide attempt histories were significantly associated with the presence of a cluster "B" co-diagnosis while controlling for childhood abuse histories, comorbid substance abuse, or current levels of depression.  
Conclusions: Cluster "B" personality disorders complicate illness course in about one-third of DSM-IV bipolar patients, making an independent contribution to increased lifetime suicide risk.  
References:  

NR25  Monday, May 3, 9:00 a.m.-10:30 a.m.  
Do Antidepressants Improve Remission in Patients With Bipolar Disorder?  
Tamara B. Pardo, B.A., Psychiatry Department, Cambridge Hospital, 1493 Cambridge Street, Cambridge, MA 02139; S. Nassir Ghaemi, M.D., Rif S. El-Mallakh, M.D., Claudia F. Baldassano, M.D., Michael J. Ostacher, M.D., Frederick K. Goodwin, M.D., Ross J. Baldessarini, M.D.  
Educational Objectives:  
At the conclusion of this session, the participant should be able to understand the long-term effects of antidepressant use in bipolar disorder.  
Summary:  
Objective: Chronic subsyndromal depression is the major morbidity of bipolar disorder (1). The long-term utility of antidepressants (AD) in reducing chronic depressive morbidity in bipolar disorder is not known (2). We report interim data from the first randomized study with modern antidepressants on this question.  
Method: An interim analysis was conducted at halfway point of a 5-year study (n=33). Subjects first recovered from a major depressive episode for 2 months (on mood stabilizer plus antidepressant), then were openly randomized to either continue (n=14) or discontinue (n=19) AD (up to 1 year follow-up presented). Remission was defined as <2 DSM-IV mood criteria within the week prior to the visit (using methods of the Systematic Treatment Enhancement Program for Bipolar Disorder study, STEP-BD).  
Results: Time in remission was similar in the AD discontinuation (74.2% of first year follow-up) versus continuation (67.3%) groups, after adjustment for potential confounders (rapid cycling, gender, substance abuse, psychiatric, and antidepressant attitude) ($\beta=2.20$, 95% CI [-23.2, 27.6]).
Conclusions: These interim data suggest that AD continuation does not lead to increased time in remission in bipolar disorder, compared to AD discontinuation.

References:

NR26 Monday, May 3, 9:00 a.m.-10:30 a.m.
Antidepressant Discontinuation and Mood Episode Relapse in Bipolar Disorder

Douglas J. Hsu, B.S., Department of Psychiatry, Cambridge Health Alliance, 1493 Cambridge Street, Cambridge, MA 02139; S. Nassir Ghaemi, M.D., Rif S. El-Mallakh, M.D., Claudia F. Baldassano, M.D., Michael J. Ostacher, M.D., Frederick K. Goodwin, M.D., Ross J. Baldessarini, M.D.

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

Summary:
Objective: In a recent observational study, antidepressant continuation (using modern antidepressants) delayed relapse versus antidepressant discontinuation following recovery from bipolar depression (1). The only previous randomized study, conducted with TCAs, found no increased relapse with antidepressant discontinuation (2). We report interim data from the first randomized study with modern antidepressants on this question.
Method: An interim analysis was conducted at halfway point of a 5-year study (n=33). Subjects first recovered from a major depressive episode for 2 months (on mood stabilizer plus antidepressant), then were randomly assigned to either continue (LT; n=14) or discontinue (ST; n=19) antidepressants (up to 1 year follow-up presented).
Results: In an unadjusted survival analysis of time to first mood episode, there was nonsignificant benefit in the LT group versus the ST group (HR=1.59±0.81, 95% Cl [0.58, 4.31]). After adjusting for confounders (rapid cycling, gender, attitude towards antidepressants), there were no notable differences in the two groups (HR=1.21±0.73, 95% Cl [0.37, 3.97]).
Conclusions: Observational evidence of increased risk of rapid depressive relapse with antidepressant discontinuation in bipolar disorder is likely to be confounding factors. Randomization and adjustment for confounders suggests little evidence of increased risk of depressive relapse with antidepressant discontinuation, even with modern antidepressants.

References:

NR27 Monday, May 3, 9:00 a.m.-10:30 a.m.
Risk for Recurrent Depression During the Postpartum Period: A Prospective Study
Ruta M. Nonacs, M.D., Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC 815, Boston, MA 02114; Lee S. Cohen, M.D., Adele C. Viguera, M.D., Alison Reminick, B.A., Bernard L. Harlow, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize clinical and demographic variables that put women with recurrent major depression at risk for postpartum depression.

Summary:
Background: The postpartum period is a time of heightened risk for psychiatric illness, particularly in women who have histories of depression. Given the prevalence of depressive disorders during the childbearing years and the negative effect of maternal depression on child development, it is crucial to identify those women at highest risk for depression during the postpartum period.
Methods: The authors prospectively followed 47 women with histories of pre-gravid DSM-IV major depression across pregnancy and into the postpartum period. Predictors of puerperal mood disturbance, including demographic and clinical variables, were examined.
Results: 48.9% of the women experienced a major depressive episode within three months following delivery. Higher rates of postpartum depression were observed in women with histories of postpartum depression and greater number of previous depressive episodes; however, these findings were not statistically significant. Women who experienced a recurrence of depression during pregnancy were at greatest risk for postpartum depression, particularly when the episode occurred proximate to delivery.
Conclusions: Women with histories of pre-gravid major depression are at high risk for relapse during the postpartum period, particularly if they experience depression during pregnancy. This population may be candidates for prophylactic interventions which may attenuate the risk of postpartum psychiatric illness.

References:

NR28 Monday, May 3, 9:00 a.m.-10:30 a.m.
Treating Subsyndromal Symptoms to Prevent Affective Relapse

Calvin K. Yang, Psychiatry Department, University of Pennsylvania, 226 W. Rittenhouse Square, 604, Philadelphia, PA 19103; Claudia F. Baldassano, M.D., Mohit P. Chopra, M.D., Laszlo Gyulai, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to evaluate the hypothesis that the pharmacologic treatment of subsyndromal symptoms in patients with bipolar I or II disorder may prevent major affective relapse.
Summary:

Introduction: Studies have shown that both subsyndromal mania and subsyndromal depression in patients with bipolar I are predictive of major affective relapse with subsyndromal mania being more predictive of relapse than subsyndromal depression. However, no studies to date have investigated whether the pharmacologic treatment of subsyndromal symptoms can prevent affective relapse in patients with bipolar disorder. This study evaluates the protective effects of pharmacologically treating subsyndromal symptoms in bipolar patients.

Methods: A database of 75 episodes of subsyndromal episodes will be included in the analysis. Subsyndromal episodes were defined by STEP-BD (Systematic Treatment Enhancement Program for Bipolar Disorder) protocol as the occurrence of ≥ 3 moderate symptoms that do not meet DSM-IV criteria for manic, mixed, or depressive episodes following a period of at least 8 consecutive weeks with no more than 2 moderate symptoms. With each subsyndromal episode, medication changes were recorded. Patients were evaluated for affective relapse using DSM-IV criteria.

Results: To date, a database of 163 patients has been systematically examined and 41 subsyndromal episodes with follow-up were identified across 29 patients. The sample included 13 men and 16 women, 26 bipolar type I and 3 bipolar type II. Analysis showed that 10/11 untreated subsyndromal episodes resulted in recovery while 22/30 treated subsyndromal episodes resulted in recovery. No significant difference was found in relapse rate between treated and untreated patients (Pearson Chi-Square, p = .234, df=1).

Conclusion: Treating subsyndromal manic, depressive, or mixed episodes may not protect against affective relapse in bipolar disorder.

References:

NR29 Monday, May 3, 9:00 a.m.-10:30 a.m.
Risk Factors for Insulin Resistance and Depression: Analysis of NHANES I
James E. Gangwisch, Ph.D., Public Health Department, Columbia University, 614 West 114th Street, New York, NY 10025

Educational Objectives:
From this session, the participant should be able to recognize the bidirectional relationship between insulin resistance and depression with depressed individuals engaging in poor health practice behaviors and with insulin resistance contributing toward depression by impairing insulin’s ability to promote brain serotonin synthesis and to suppress the reuptake of norepinephrine.

Summary:
Introduction/Hypothesis: Many depressed individuals have been found to engage in behaviors that are known risk factors for insulin resistance (IR). Cortisol release from stress has also been shown to have deleterious effects upon both insulin sensitivity and mood. This study was conducted to see whether individuals who are likely to suffer from insulin resistance based upon engagement in poor health practice behaviors would be more likely to suffer from depression while controlling for stress.

Methods: Logistic regression was used to examine the relationship between depression and the likelihood of being IR (based upon measures of risk factors for IR: BMI, hours sleep per night, physical activity, sweets consumption, and alcohol consumption) while controlling for stress.

Results: Subjects likely to be IR were 45% more likely to be depressed (odds ratio = 1.45; 95% CI = 1.28 to 1.63; p = .0001) than subjects unlikely to be IR after controlling for stress.

Conclusions/Discussion: Subjects likely to be IR have increased rates of depression, which is consistent with findings that individuals with diabetes and cardiovascular disease are at greater risk of depression. This relationship is likely to be bidirectional, with depressed individuals being more likely to engage in poor health practice behaviors and with IR contributing toward depressed mood by impairing insulin’s ability to promote brain serotonin synthesis and to suppress the reuptake of norepinephrine.

References:

NR30 Monday, May 3, 9:00 a.m.-10:30 a.m.
Increased Delta Power Across NREMS Episodes in Women With Major Depression
Xavier A. Preud’Homme, M.D., Psychiatry Department, Duke University Medical Center, Box 3837, Durham, NC 27710; Andrew D. Krystal, M.D., Jean P. Lanquart, Ph.D., Paul Linkowski, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to understand the effect of gender on EEG slow wave activity patterning across non-rapid eye movement sleep episodes in depressed vs. healthy subjects.

Summary:
Background: Depression is classically associated with lower EEG-delta activity across NREMS episodes and without the usual monotonic exponential declining pattern. However, Armitage and co-workers indicated that this was not the case.

Methods: To further explore this controversial issue, we investigated slow wave activity (SWA) patterning across consecutive non-rapid eye movement sleep (NREMS) episodes within seventeen psychotropic-free major depressed patients matched for age and gender with medication-free healthy subjects over three nights. SWA was estimated by computing spectral estimates of the EEG signal using Fast Fourier Transform and generating measures of delta power.

Results: Surprisingly, we found that SWA per NREMS episode was greater for depressed women vs. healthy subjects. In addition, in agreement with Armitage et al, we found that SWA declines exponentially across the first four NREMS episodes comparatively with the patterning observed for normatives and in contrast with the generally held view.

Conclusion: Contrary to the prevailing idea of decreased delta activity associated with depression, our data support that, in depressed women, SWA is increased while it conserves its classic monotonic exponential declining pattern across NREMS episodes. This suggests possible differences in the pathophysiology of depression between men and women or just different subtypes of depressed patients.
Illness Severity and Longitudinal Course in College Students With Bipolar Disorders

Anna Sapochnikova, Bard College, 1 Annandale Road, Annandale-on-Hudson, NY 12504; Rebecca A. Chandler, B.S., Andrea M. Alarcon, B.A., Po W. Wang, M.D., Cecylia Nowakowska, M.D., Wendy K. Marsh, M.D., Terence A. Ketter, M.D.

Educational Objectives:
- At the conclusion of this session, the participant should be able to recognize that college students with bipolar disorders (BD) may have expected indicators of illness severity, but generally longitudinal course with only limited use of polypharmacy.

Summary:
Objective: To assess illness severity and longitudinal course in college students with bipolar disorders (BD).
Method: Retrospective chart review.
Results: Forty-two BD (24 type I, 11 type II, 7, NOS) patients (age 21.8±3.2 years, 50% female) were treated for 1.7±1.4 years. Patients had illness onset at 16.1±4.2 years, duration 5.8±4.1 years, and were on 2.2±1.5 psychotropic medications. Prior hospitalizations (64%), suicide attempts (26%), anxiety disorders (63%), cannabis abuse (43%) and alcohol abuse (37%) were common. First treatment ever was for depression in 68%, and consisted of unopposed antidepressants in 50%, and the latter was associated with increased rate of history of pharmacological hypomania (67% vs. 21%, p<0.01). At Stanford, Clinical Global Impressions (CGI) improved from 3.3 to 2.4 (p<0.005), Global Assessment of Function increased from 59 to 67 (p<0.005), and percentage of patients in syndromal episodes fell from 48% to 12%. Patients with prior hospitalizations and suicide attempts accounted for all those with hospitalization (14%) and suicide attempts (7%) at Stanford. Patients were on 2.4±1.5 psychotropic medications at last visit.
Conclusion: BD in college students appeared associated with expected levels of illness severity, but limited polypharmacy, and generally good longitudinal course. Further studies are warranted to explore these preliminary observations.

References:

Conclusions:
- Although frequent, SUDs in early BD do not yet predict outcome in a significant way. This indicates that the early period of BD is a window of opportunity for interventions in this high-risk subgroup. The interventions should specifically address anxiety symptoms.

References:
disorder. The proportion with a family history did not vary by sex of proband, but patients aged less than 46 were more likely to have an affected relative (p=0.02). The number of affected relatives was high, with 29.3% of probands having two or more affected relatives; 17.9% of probands had at least one relative with bipolar disorder, 29.3% with depression, 16.3% with schizophrenia and 6.5% with alcohol abuse.

Conclusions: Our results, although preliminary, are consistent with those from other studies. Community-based mental health clinics are well placed to identify susceptible relatives and develop intervention strategies.

References:
2. Rucci P, Frank E: Suicide attempts in patients with bipolar I disorder during acute and maintenance phases of intensive treatment with pharmacotherapy and adjunctive psychotherapy. Am J Psychiatry 2000; 1180-1184

NR34 Monday, May 3, 9:00 a.m.-10:30 a.m.
Depressive Symptoms in Geriatric Caregivers of Acute Stroke Patients
Gary P. Epstein-Lubow, M.D., Psychiatry Department, Brown University, Butler Hospital, 345 Blackstone Boulevard, Providence, RI 02906; Duane S. Bishop, M.D., Ivan W. Miller, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize that caregivers of stroke survivors are at risk for depression, and this risk is increased if family functioning is poor.

Summary:
Background: Family Intervention: Telephone Tracking (FIT) is an investigation of a telephone-administered family treatment for stroke patients and their caregivers. The purpose of this report is to describe caregivers' depressive symptoms and family functioning soon after their family member's acute stroke.

Methods: Measures included caregivers' depressive symptoms and family functioning (Family Assessment Device [FAD]), and additional scales designed to assess perceived health status, life satisfaction and stroke patients' functional impairment.

Results: Baseline data were analyzed for 54 caregivers ages 60 to 87 (Mean Age 72, SD = 7.0). The mean score on the CES-D was 12.4 (SD = 10.5). Depressive symptoms were mild (15 < CES-D < 23) in 15% and severe (22 < CES-D) in 15% of caregivers. Families were assessed to have healthy functioning in 70% of cases (Mean FAD General Functioning 1.8, SD = 0.5 [“healthy” <2.1]). Depressive symptoms in caregivers were significantly correlated with level of family functioning (r = .39, p < .01).

Conclusions: Thirty percent of caregivers experienced significant depressive symptoms during their loved one's recovery from stroke. Depressive symptoms in caregivers were correlated with worse family functioning.

References:

NR35 Monday, May 3, 9:00 a.m.-10:30 a.m.
Double-Blind, Placebo-Controlled Trial of Mexiletine for Mania or Hypomania
Ayal Schaffer, M.D., Department of Psychiatry, Sunnybrook and WCHSC, 2075 Bayview Avenue, Room FG46, Toronto, ON M4N 3M5, Canada; Anthony J. Levitt, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to become more aware of the potential use of the anticonvulsant mexiletine for the treatment of bipolar disorder.

Summary:
Objective: Mexiletine hydrochloride is an anticonvulsant with a similar mechanism of action to currently used mood stabilizers. Open-label data has suggested efficacy of mexiletine for treatment-resistant bipolar disorder. The purpose of this study was to identify whether mexiletine is efficacious and safe for the treatment of mania or hypomania.

Method: A 3-week randomized, double-blind, placebo-controlled, add-on study in bipolar disorder (BD) patients with current hypomania or mania. Patients remained on their baseline medications throughout the course of the study.

Results: Ten subjects (3 female, 7 male) outpatients were enrolled in the study. Six subjects with BD type I, and four subjects with BD type II. There was no significant difference in age (mean age = 46.9 years, SD = 9.4) or baseline YMRS score between the treatment groups. Mean change in YMRS score among subjects on mexiletine compared to placebo was -12.4 versus -9.6, respectively. Mexiletine was generally well tolerated, and there were no serious adverse events.

Conclusions: This pilot study suggests that mexiletine hydrochloride may be an efficacious treatment for some patients with bipolar disorder. Larger trials are required to confirm these results.

References:

NR36 Monday, May 3, 9:00 a.m.-10:30 a.m.
Clinical Correlates of Current Level of Functioning in Bipolar Patients
Tomas Hajek, M.D., Psychiatry Department, Dalhousie University, 5909 Veteran's Memorial Lane, Halifax, NS B3H 2E2, Canada; Claire Slaney, R.N., Julie Garnham, B.S.N., Martina Ruzicacova, M.D., Michael Passmore, M.D., Martin Alda, M.D.

Educational Objectives:
At the end of this presentation, the participants will have information about variables associated with decreased functioning in bipolar disorder.

Summary:
Objective: Bipolar disorder is a serious medical condition decreasing occupational and social functioning. This study examined clinical correlates of impaired functioning in a large, well-characterised community sample of bipolar patients.

Method: 252 patients from the Maritime Bipolar Registry, with DSM-IV diagnoses of bipolar I or bipolar II disorder, participated in the study. Global assessment of functioning (GAF) was compared across clinical and demographic variables.

Results: Lower GAF scores were found in patients with chronic illness course, rapid cycling, history of suicidal behaviour, psychiatric comorbidity, thyroid dysfunction and diabetes mellitus. There were no differences in level of functioning between men and
women, bipolar I and bipolar II patients, patients with and without psychotic episodes or hypertension.

Conclusions: Functioning in bipolar patients is decreased not only due to specific disorder related variables, but also due to frequent comorbidity with other psychiatric and general medical conditions.

References:


NR37

Prevalence and Incidence Rates and Comorbidity Among Patients With Bipolar Disorder Supported by Bristol-Meyers-Squibb

Jeff J. Guo, Ph.D., Pharmacy Department, University of Cincinnati, 3223 Eden Avenue, Cincinnati, OH 45267; Paul E. Keck, Jr., M.D., Raymond Jang, Ph.D., Hong Li, Ph.D., Dong Ming Jiang, M.S., Carson Williams, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to describe prevalence and incidence rates, and comorbidities for patients with bipolar disorders in a managed care Medicaid population.

Summary:

Objective: To identify prevalence and incidence rates of bipolar disorders, and to categorize medical comorbidities among patients with bipolar disorders in a managed care Medicaid population.

Methods: Using a multi-state claims database, patients who had at least 3-months continuous enrollment and at least one bipolar diagnosis indicated by ICD9 codes 296.0x, 296.1x, 296.4x, 296.5x, 296.6x, 296.7x, 296.8x, and 301.13 were selected from 1/1/1998 to 12/31/2002.

Results: The monthly prevalence rates of bipolar disorder increased by age with age 35-49 years old being the peak (2.1%). Of 13,996 identified bipolar patients, 64.2% were female with an average of age 29.4 (SD 13.8). Life-time bipolar diagnostic categories included 88.17% bipolar I, and 11.83% bipolar II. Patient's last bipolar diagnoses indicated 4.95% with psychosis, 12.8% with manic, 58.1% with mixed, 22% with depression, and 7.1% with hypomanic. Severity categories were 11% severe, 8.6% moderate, 2.1% mild, 2.2% remission, and 76.1% unspecified.

Key comorbidities of psychiatric disorders included previous major depressive 41.7%, anxiety disorder 36.1%, alcohol use disorder 8.2%, substance use disorder 9.6%, and personality disorder 4.5%. General comorbidities included hypertension 13%, diabetes mellitus 7.2%, obesity 7.9%, COPD 4%, arthritis 1.5%, neoplasm 0.4%, ischemic heart disease 2.2%, and cerebral vascular diseases 1.7%.

References:


NR38

Physician Prescribing Patterns in 100 Bipolar Depressive Episodes

Alice G. Chang, M.D., Psychiatry Department, Hospital of the University of Pennsylvania, 8201 Henry Avenue #12, Philadelphia, PA 19128; Claudia F. Baldassano, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to evaluate physician prescribing patterns and to study the efficacy of particular classes of medications in treating bipolar depression.

Summary:

Introduction: Although bipolar depression is the most difficult phase of bipolar disorder to treat and a major cause of morbidity and mortality, it has not been sufficiently studied. There is data to suggest antidepressants may have a negative impact on the short- and long-term course of bipolar illness precipitating manic switch or cycle acceleration. This study evaluates physician prescribing practices for acute bipolar depression and secondary assesses outcomes.

Methods: We systematically assess 100 episodes of depression in patients with DSM-IV diagnosis of bipolar disorder. We evaluate whether a history of rapid-cycling, antidepressant-induced mania, severity of illness and bipolar type, affect psychiatrist's choice in treating bipolar depression. Clinical response is assessed based on prospective application of the Clinical Global Impression scale (CGI), and the Global Assessment of Functioning scale (GAF) at 8 weeks of treatment.

Preliminary Results: Eighty-two episodes have been collected to date. The sample included 46 men and 54 women, 68 bipolar type I and 14 bipolar type II. 43/82 (52.4%) of the sample had a history of antidepressant-induced switch, and 60/82 (73%) had a lifetime history of rapid cycling. 47.5% of patients were treated with an antidepressant; 47.5% with an antiepileptic, and 29.2% with an atypical antipsychotic.

Conclusion: We did not find any factors that impacted on physician prescribing practices suggesting that real-world practice is driven by factors other than the existing literature.

References:


NR39

Effectiveness of Antidepressant Medication Prescribed at Primary Care

Antoni Serrano, M.D., Department of Research, Sant Joan de Deu - SSM, Dr Antoni Pujadas 42, Sant Boi de Llobre 08830, Spain; Alejandra Pinto-Meza, B.A., Josep M. Haro, M.D., Elena Blanco, M.D., Nuria Lara, M.D., Carmen Perez, M.D., Cristina Moliner, M.D.

Educational Objectives:

At the conclusion of this session, different antidepressants used for treating major depression at primary care show similar effectiveness and discontinuation frequencies

Summary:

Objective: To assess effectiveness of antidepressant medication prescribed for treating major depression (MD) in 13 primary care centers (PCC).
Method: From a total sample of 333 subjects (aged 18-75) followed-up during six months after receiving an antidepressant (prescribed by their primary care physician because they were believed to have a depressive disorder), 118 had a MD episode. At baseline, after 3, and 6 months, subjects were interviewed by telephone in order to assess sociodemographics, DSM-IV diagnostic criteria, depression severity (PHQ-9 scale by Kroenke et al., 2001), and treatment compliance. 110 subjects with MD completed the follow-up period. Main outcome measure was symptoms reduction.

Results: 73.7% were women. Mean age was 44.71 years old (SD 13.07). Fluoxetine was the more frequently prescribed antidepressant (33.9%), followed by Paroxetine (31.4%), Citalopram (14.4%) and Sertraline (12.7%). Treatment discontinuation frequencies were 30.4% after 3 and 40.9% after 6 months (no differences were observed among treatment groups). There was a significant reduction of symptoms in all treatment groups after 3 and 6 months, but no differences were observed among them.

Conclusions: SSRI are the most prescribed for treating MD, Fluoxetine, Paroxetine, Citalopram and Sertraline have similar discontinuation frequencies and effectiveness for treating MD.

References:

NR40  Monday, May 3, 9:00 a.m.-10:30 a.m.
A Prospective, Longitudinal Study of Seasonality in African Students Living in the Greater Washington, D.C., Metropolitan Area
Ryszard Zebrak, M.D., Barton Hall, St. Elizabeth Hospital, 2700 Martin L. King Avenue, Room 200, Washington, DC 20032; Irighad A. Sumar, M.D., Kelly J. Rohan, Ph.D., Alvaro Guzman, M.D., John W. Stiller, M.D., Courtney M. Thrower, M.A., Teodor T. Postolache, M.D.

Educational Objectives:
At the conclusion of this session, the participants may be able to estimate degree of seasonal changes in person using variations in weight over the seasons.

Summary:
Objectives: This is a prospective, longitudinal study of seasonality in a vulnerable population, i.e., Africans. Because of serotonin role in mood and appetite/weight regulation and seasonal variation in brain serotonin turn over, we hypothesized that mood and energy would be lower and appetite and weight would be higher in fall and winter.

Methods: Four cohorts of volunteering African students (N = 161) attending a year-long nursing school in Washington, DC, were assessed monthly for 1 year. Forty-three subjects (M age = 33.46±6.25) predominantly females (76.7%), completed study. The cohorts began their academic program in different seasons inherently minimizing confounding influences on seasonality. Assessments concluded visual analog scales and weight on a digital scale. For each standardized dependent variable, averages for spring/summer and fall/winter were compared using paired t-tests.

Results: As expected, body weight was significantly higher in fall/winter, p < .001. Students demonstrated a trend towards increased appetite in fall/winter p < .10.

Conclusions: In this sample, prospective measurements of body weight and self-reported appetite appeared to be a sensitive indicator of seasonality. Our results are consistent with the literature on seasonal variation of serotonin turnover in the brain and the role of serotonin on appetite and weight regulation.

References:

NR41  Monday, May 3, 9:00 a.m.-10:30 a.m.
Birth Seasonality in Fall-Winter Depression
Edda Pjaks, M.D., General Psychiatry Department, University of Vienna, Wehringr Gervelt 18-20, Vienna 1090, Austria; Dietmar Winkler, M.D., Anastasios Konstantinouis, M.D., Angela Heiden, M.D., Siegfried Kasper, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize, that seasonality of birth is not only present in schizophrenia but also in seasonal affective disorder.

Summary:
Objective: Season of birth is a putative etiological factor for several psychiatric illnesses [1]. The aim of this investigation was to examine seasonal differences in the frequency of birth in a sample of patients with seasonal affective disorder (SAD).

Methods: 553 outpatients suffering from SAD, winter type, were included in this evaluation. We compared the observed number of births in our sample with expected values calculated from the general population.

Results: There was a significant deviation of the observed number of births from the expected values on a monthly basis (p<0.01). We also found less births than expected in the first quarter of the year and a slight excess of births in the second and third quarter (p<0.05). Interestingly, patients with melancholic depression were more frequently born in fall/winter and less often in spring/summer compared to patients with atypical depression (p<0.01).

Conclusions: For the pathogenesis of SAD genetic factors [2] and also environmental circumstances such as birth seasonality seem to be important. In addition birth effects seem to be dependent on the symptom profile of the patients, but further studies are needed to elucidate the underlying mechanisms of these observations.

References:

NR42  Monday, May 3, 9:00 a.m.-10:30 a.m.
Serum-Iron and Serum-Albumin in MDD
John W. Denninger, M.D., Department of Psychiatry, Massachusetts General Hospital, 50 Stanford Street, Suite 401, Boston, MA 02114; George I. Papakostas, M.D., Eliana Tossani, Ph.D., Erin C. Beaumont, B.A., David Mischoulon, M.D., Jonathan E. Alpert, M.D., Maurizio Fava, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the relationships between serum iron, serum albumin
levels, depression severity and clinical response in major depression.

Summary:

Background: The importance of biochemical markers such as serum iron and serum albumin in major depressive disorder (MDD) is unclear. We sought to examine the effect of baseline serum iron and serum albumin on depression severity and antidepressant response in MDD.

Methods: 308 MDD outpatients (39.5 ± 10.4 years; 168 women) enrolled in an 8-week, 20mg, open trial of fluoxetine had serum iron, serum albumin, height and weight measured at baseline. We assessed the relationship of serum iron and albumin levels at baseline to: 1) depression severity at baseline (as measured by the 17-item Hamilton Depression Rating Scale [HAM-D-17] total score), controlling for age, gender, and BMI, and 2) clinical response, controlling for baseline HAM-D-17.

Results: In a multiple regression controlling for age, gender and BMI, lower serum albumin levels predicted greater baseline HAM-D-17 scores (p<0.02); serum iron levels did not predict baseline HAM-D-17 scores (p>0.05). Neither baseline serum iron nor serum albumin levels predicted fluoxetine response (p>0.05).

Conclusion: In this open trial of fluoxetine in 308 MDD outpatients, serum albumin predicted greater baseline depression severity, but not clinical response. Serum iron, on the other hand, did not significantly predict either baseline depression severity or clinical response. Future studies on the role of these markers in MDD are warranted.

References:


**NR44** Monday, May 3, 9:00 a.m.-10:30 a.m.
Assessment of the Mood Disorder Questionnaire in a Forensic Setting
Omar Elhaj, M.D., Psychiatry Department, Case Western School of Medicine, 11400 Euclid Avenue, Suite 200, Cleveland, OH 44106; Eric A. Youngstrom, Ph.D., Heather E. Sakai, M.S., Kristene A. Packer, B.A., Sarah R. Bilali, M.A., Robert L. Finding, M.D., Joseph R. Calabrese, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to assess the validity of the Mood Disorder Questionnaire (MDQ) in a forensic setting.

Summary:

Background: The MDQ is a screening instrument for bipolar disorder (BD) that has previously been validated in the psychiatric outpatient and general population.

Method: During booking, each inmate in the Ottawa County Jail completes MDQ as a part of the booking procedures. Researchers then interview every consenting inmate and obtain demographic information, administer the MINI International Neuropsychiatric Interview (MINI), the alcohol/drug sections of the Structured Clinical Interview for DSM-IV (SCID), and the Addiction Severity Index.

Results: One hundred and sixty eight screens were valid for analysis. The rate of positive MDQ is (10.1%, N= 17. Sixty-nine inmates consented for the interview. The rate of BD diagnosis using MINI was (41%, N= 28)). The sensitivity of MDQ in this setting is (50%), while its specificity is (93%).

Conclusion: The sensitivity of MDQ reported in this forensic setting is lower than what was previously reported (0.5 vs. 0.73), while its specificity remained closely high (0.93 vs. 0.9). Since specificity is high and sensitivity is mediocre, it is likely that the prevalence of BD is between 10% and 40%.

References:


2. Regier, D; Farmer, M; Rae, D; et al: Comorbidity of mental disorders with alcohol and other drug abuse. JAMA 1990; 264:2511-2518.
NR45  Monday, May 3, 9:00 a.m.-10:30 a.m.
The Prevalence of Bipolar and Comorbid Disorders in the Ottawa County Jail
Omar Elhaj, M.D., Psychiatry Department, Case Western School of Medicine, 11400 Euclid Avenue, Suite 200, Cleveland, OH 44106; Eric A. Youngstrom, Ph.D., Heather E. Sakai, M.S., Kristene A. Packer, B.A., Sarah R. Bilali, M.A., Robert L. Finding, M.D., Joseph R. Calabrese, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to assess the prevalence of Bipolar Disorder (BD) and its comorbidity in jail inmates.

Summary:
Method: During booking, each inmate completes the Mood Disorder Questionnaire (MDQ) and Michigan Alcohol Screening Test (MAST). Researchers then interview every consenting inmate and obtain demographic information, administer the MINI International Neuropsychiatric Interview (MINI), the alcohol/drug sections of the Structured Clinical Interview for DSM-IV (SCID), and the Addiction Severity Index.

Results: Sixty-nine inmates consented to be interviewed. Seventy-five percent of the consenting sample had a negative MDQ score. The prevalence rates assessed using the MINI and SCID are: 41% for BD, of which 86% is Bipolar I disorder. The rate of comorbid anxiety disorders is 75%. The rate of comorbid substance use disorders (SUD) in BD is 93%. The rate of anxiety disorders (AD) in the dual-diagnosis sub-sample is 70%. Of those who qualified for a diagnosis of BD, 39% had previously been correctly diagnosed. The mean delay in receiving a diagnosis of BD since symptom onset is 15 years.

Conclusion: A high prevalence rate of BD is observed in this inmate sample. The majority of inmates with BD present comorbid with either SUD or AD. Most of the cases are undiagnosed and untreated.

References:

NR46  Monday, May 3, 9:00 a.m.-10:30 a.m.
Identifying the Mentally Ill in the Ottawa County Jail: A Screening Project
Omar Elhaj, M.D., Psychiatry Department, Case Western School of Medicine, 11400 Euclid Avenue, Suite 200, Cleveland, OH 44106; Eric A. Youngstrom, Ph.D., Heather E. Sakai, M.S., Kristene A. Packer, B.A., Sarah R. Bilali, M.A., Robert L. Finding, M.D., Joseph R. Calabrese, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to assess the prevalence of Mental Illness (MI) and Substance Use Disorders (SUD) in jail inmates.

Summary:
Methods: During booking, each inmate completes the Mood Disorder Questionnaire (MDQ) and Michigan Alcohol Screening Test (MAST). Researchers then interview every consenting inmate and obtain demographic information, administer the MINI International Neuropsychiatric Interview, the alcohol/drug sections of the Structured Clinical Interview for DSM-IV, and the Addiction Severity Index.

Results: Of 168 analyzable MDQ’s, 16 inmates (10%) met criteria for a positive MDQ score and of 188 analyzable MAST’s, 64% met criteria for having a borderline or definite problem with alcohol/drug use. Of the 69 inmates who consented to interviews, most were Caucasian males with a mean age of 33 years; 94% were diagnosed with a SUD or MI, 90% with a SUD, and 57% with a MI. Bipolar Disorder (42%), Unipolar Depression (8%), and Schizophrenia (6%); 36% were diagnosed with an Anxiety Disorder including Post Traumatic Stress Disorder (26%), Generalized Anxiety Disorder (16%) and Panic Disorder (15%).

Conclusion: The majority of inmates interviewed have either a SUD or MI. The recognition and treatment of this population remains an important public health issue that needs to be addressed further.

References:

NR47  Monday, May 3, 9:00 a.m.-10:30 a.m.
Smoking Patterns Across Psychiatric Disorders: How Often Do We Tell Our Patients to Stop?
Yvette M. Cruz, M.D., Psychiatry Department, Hospital of University of Pennsylvania, 3535 Market Street, 2nd Floor, Philadelphia, PA 19104; Claudia F. Baldassano, M.D., John P. O’Reardon, M.D., Jeffrey P. Staab, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to evaluate the prevalence of smoking in psychiatric patients and to assess how often smoking cessation is recommended by the psychiatrist.

Summary:
Introduction: Persons with psychiatric illnesses are about twice as likely as the general population to smoke tobacco. They also tend to smoke more heavily than other smokers. Data suggest that quit rates in patients with psychiatric disorders is similar to the general population. How often psychiatrists promote smoking cessation is not known.

Methods: To investigate the prevalence of cigarette smoking, 300 psychiatric outpatients with anxiety disorders, unipolar depression and bipolar disorder complete a self-evaluation questionnaire about smoking behavior including attempts to quit and whether this was a recommendation from the treating psychiatrist. Attitudes about smoking are included in the questionnaire. A separate questionnaire is administered to psychiatrists evaluating whether they recommend smoking cessation and how often smoking is addressed as a part of treatment.

Results: Prevalence of smoking will be compared among the psychiatric disorders. Among 100 bipolar patients, for whom we already have data, the lifetime prevalence of smoking is 48% and current smoking is 35%. How frequently psychiatrists recommend smoking cessation will be analyzed. In addition, patients’ attitudes toward smoking will be assessed.

Conclusion: Smoking is a major public health problem and since prevalence rates are higher in our psychiatric patients, psychiatrists should devote more effort to smoking cessation.

References:
NR48  Monday, May 3, 9:00 a.m.-10:30 a.m.
Development of a HAM-D/MADRS Depression Rating Interview
Rebecca Iannuzzo, Ph.D., CENORR, Zucker Hillside Hospital, 75-59 263rd Street, Glen Oaks, NY 11004; Judith Jaeger, Ph.D., Joseph F. Goldberg, M.D., Vivian Kafantaris, M.D., M. Elizabeth Sublette, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the scientific and clinical advantages of rating depression using a combined HAM-D and MADRS interview questionnaire.

Summary:

Objective: The Hamilton Rating Scale for Depression (HAM-D) is the most widely used measure in depression research despite its methodological shortcomings (including limited sensitivity to changes in depression severity, low item reliability, heavy weighting toward somatic/behavioral symptoms). In response to these criticisms, modified versions have been developed (i.e. including subscale and expanded versions, structured interviews to standardize administration etc.). However, a lack of clarification in the literature as to what version, administration type and scoring procedures were used prevents interpretation and comparison of data. The Montgomery-Asberg Depression Rating Scale (MADRS), also used in depression research, was designed to have greater sensitivity to changes in depression due to antidepressant treatment.

Method: We developed a new instrument in which items from the MADRS and the 21-, 24-, and 31-item versions of the HAM-D were integrated into a single interview questionnaire consisting of 43 items (10 MADRS and 33 HAM-D items). The semi-structured interview is based on HAM-D questionnaires (21- and 24-item). Data collection and establishment of inter-rater reliability are currently underway.

Conclusions: Resulting data will permit us to compare the psychometric properties of the HAM-D and MADRS using a single interview, and allow depression researchers to efficiently administer both instruments.

References:

NR49  Monday, May 3, 9:00 a.m.-10:30 a.m.
Comorbidity of Anxiety Disorders in Dysthymic Disorder
Cristina Toba, M.D., Psychiatry Department, St. Luke’s Roosevelt, 910 Ninth Avenue, New York, NY 10019; David J. Hellerstein, M.D., Sarai Batchelder, Ph.D., Edwin S. Meresh, M.D., Steven E. Hyler, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize and describe the comorbidity between AD and DD and the implications for treatment.

Summary:

Objective: To analyse the relationship between the Phospholipase A2 (PLA2A) gene and Borderline Personality Disorder (BPD) in opioid dependence using the temperament dimensions described by Cloninger. This gene was selected because of a previously described relationship with Bipolar Disorder, an axis I affective disorder.

Method: Cross-sectional study of 128 opioid dependent subjects admitted to an inpatient Detoxification Unit. The International Personality Disorder Examination (IPDE) and the Temperament and Character Inventory (TCI) of Cloninger were used. The variants of the PLA2A gene were examined by PCR amplification of DNA.
extracted from oral cells and correlated with the temperament dimensions using the Spearman Test.

Results: 45.3% of the patients had at least one Personality Disorder (PD). The Non-Specified PD was the most prevalent (15.6%), followed by Antisocial (13.3%) and Borderline (BPD) (11.7%). Mean values for the temperamental dimensions were 21.9 in novelty seeking, 17.1 in harm avoidance (HA), 15.2 in reward dependence and 4.6 in persistence. For the character dimensions of personality, 24.3 was obtained in self-directedness, 28.3 in cooperativeness and 17.9 in self-transcendence. Only the HA’s dimension was correlated with the PLA2A variants (R=0.272=0.020).

Conclusions: recent studies have shown that the dimension of HA is related with BPD by low scores and this dimension has been correlated in this study with the PLA2A gene. Therefore, this gene should be explored in future studies as a potential BPD marker.

References:

NR51 Monday, May 3, 9:00 a.m.-10:30 a.m.
A Delusional Disorder Case Register Study
Nieves C. Gonzalez, Research Department, Sant Joan de Deu - SSM, Dr. Antoni Pujadas 42, Sant Boi de llobre 08830, Spain; Nuria Orcero, Enrique de Portugal, Jorge Cervilla, Ph.D.

Educational Objectives:
At the conclusion of this session, among delusional disorder subtypes, persecutory subtype is the most frequent in all the variables analysed in this study.

Summary:
Objectives: To quantify and identify Delusional Disorder (DD) cases and subtypes, to study the comorbidity with other Axis I and personality disorders, as well to assess (GAF) functioning and use of sanitary resources.

Methods: We set up a case register of DDs diagnosed among all patients attending to mental health services (700,000 inhabitants) provided by SJD-SSM in Barcelona, Spain. A total sample of 407 patients with established DSM-IV diagnosis of DD was included during the 5-year period during which our study has spanned. We also assessed sociodemographics, emergency and hospital consultations, and GAF level. We made an analysis description among subtypes.

Results: n=407 patients, 56.5% are women. Mean age is 53 years old. Mean use of resources is 34%, being more frequent persecutory subtype (47%) followed by NOS and mixed subtypes. 45% GAF shows low level of general functionality. We also found significant differences in comorbidity with other Axis I and II disorders (persecutory and jealous subtypes associated with depressive disorder in a 33% and 50% of somatic subtype with anxiety disorders) Cluster A most frequent in all subtypes.

Conclusions: Persecutory subtype is the most frequent among subtypes, with the better GAF level, but with higher number of hospitalization.

References:


NR52 Monday, May 3, 9:00 a.m.-10:30 a.m.
Association Study of Dysbindin Gene With Schizophrenia
Aida T. Ruiz, M.D., Department of Psychiatry, University of Chile, Avenida La Paz 1003, Santiago 700-10, Chile; Pak Sham, M.D., John Powell, Ph.D., Tao Li, M.D., Eduardo Miranda, M.D., Carlos Encina, M.D., Mario Quijada, M.D., Robin M. Murray, M.B.

Educational Objectives:
At the conclusion of this session, the participant should be able to understand association genetics studies, using a case-control design, to analyze candidate genes in schizophrenia.

Summary:
Objective: Evidence for association between genetic variants in the dysbindin gene, on 6p22.3, and schizophrenia has been recently described. The objective of this study was to conduct an association analysis of dysbindin gene in a Chilean sample.

Method: One hundred and twelve schizophrenic patients, according to DSM-IV criteria, and 239 unaffected control individuals were collected in Santiago, Chile. Seven of the most positive SNPs reported to be associated with schizophrenia were genotyped. Linkage disequilibrium (LD) between markers was calculated using 2LD program. Association between markers and schizophrenia risk was tested, in patients and controls, using a standard X2 test. The analysis for haplotype association was performed using EH+ program.

Results: No deviation from the Hardy Weinberg equilibrium was found. Significant LD was observed for most pair wise calculations (D=0.42 - 1.00). No single marker achieved a significant allelic association (P = 0.2 - 0.9). Tests for haplotype analysis showed no association (P = 0.42).

Conclusions: In comparison with previous studies, a similar pattern of LD was found in this sample. However, association between dysbindin gene and schizophrenia was not confirmed.

References:

NR53 Monday, May 3, 9:00 a.m.-10:30 a.m.
Analysis of Association of RGS4 Genetic Variants and Schizophrenia
Aida T. Ruiz, M.D., Department of Psychiatry, University of Chile, Avenida La Paz 1003, Santiago 700-10, Chile; Pak Sham, M.D., John Powell, Ph.D., Tao Li, M.D., Eduardo Miranda, M.D., Carlos Encina, M.D., Mario Quijada, M.D., Robin M. Murray, M.B.
Educational Objectives:

At the conclusion of this session, the participant should be able to understand association genetics studies, using a case-control design, to analyze candidate genes in schizophrenia.

Summary:

Objective: Recent studies have reported that polymorphisms in the RGS4 gene, on 1q21-22, are associated with schizophrenia. This study analyzed this possible association in an ethnically different population.

Method: A case-control study of 112 cases, with DSM-IV schizophrenia, and 239 unaffected control subjects recruited in Santiago, Chile, was carried out. Three markers (SNPs), previously described to be associated with schizophrenia, were analyzed. Intermarker linkage disequilibrium (LD) was measured by means of 2LD program. SNPs were tested for association with schizophrenia using X² statistics. Haplotype analysis was performed using EH+ program.

Results: All markers were found to be in Hardy-Weinberg equilibrium, in both cases and controls. All pairs of SNPs showed strong linkage disequilibrium (D' = 0.99 - 1.00). None of the SNPs included in this analysis was found to be associated with illness (P = 0.59 - 0.96). No significant haplotypic association was observed (P = 0.18).

Conclusions: No evidence was found to support an association between genetic variants in the RGS4 gene and schizophrenia in this sample.

References:


NR54
Monday, May 3, 9:00 a.m.-10:30 a.m.
Prescribing Patterns in Treatment-Resistant Schizophrenia

Millia Begum, M.B., Department of Psychiatry, The State Hospital, Carstairs, Lanark ML 11 8BP, Scotland; Janice Janeette, B.Ph.

Educational Objectives:

At the conclusion of this session, our data suggests that clozapine as a treatment is significantly delayed in resistant cases of schizophrenia and such a delay can have major implications on clinical outcome and quality of life.

Summary:

Objective: to determine the delay in starting clozapine in patients with treatment resistant schizophrenia and analyze reasons for such a delay.

Method: The study conducted at the Argyll and Bute Hospital, Scotland as a retrospective case note review of patients who had a consistent diagnosis of schizophrenia and eventually started on clozapine. Main outcome measured as the time lag between I and II adequate trials and the time duration between the II adequate trial and start of clozapine.

Results: After exclusion, 40 patients reviewed, had a median of 5 years delay in starting clozapine (since its licensed use), with a median of 1.7 years between 2 adequate antipsychotic trials. Of the many patient and clinician factors, one of the important reason was a high rate of repeat evaluation of the same antipsychotic class (average of 2.3 class repeated). Reasons for switching antipsychotics were not well recorded. Small but significant percentage were on combination and depot preparation during start of clozapine.

Conclusion: There was significant delay in starting clozapine and giving adequate trials, reasons for which could be multiple. Every effort should be taken to minimize such delays as this can have serious long term implications on clinical outcome and quality of life.

References:


NR55
Monday, May 3, 9:00 a.m.-10:30 a.m.
Factor Structure of Delusions in Individuals With Schizophrenia

David Kimhy, Ph.D., Columbia University, Psychiatry Department, 1051 Riverside Drive, New York, NY 10032; Raymond Goetz, Ph.D., Scott Yele, M.S.W., Cheryl M. Corcoran, M.D., Dolores Malaspina, M.D.

Educational Objectives:

At the conclusion of this session, the participant will be aware that delusions are heterogeneous and are best represented by three main types: Influence, Grandeur, and Persecution.

Summary:

Introduction: To date, it remains unclear whether delusions represent a phenomenon that is neurobiologically unique from other psychotic symptoms, or even if different delusions reflect a unitary phenomenon with common neurobiological underpinnings. The present study examined the factor structure of delusions.

Method: 91 neuroleptic-free subjects with DSM-IV schizophrenia/schizoaffective disorder were assessed using the Scale for Assessment of Positive and Negative Symptoms (SAPS/SANS) and the Schedule for the Deficit Syndrome (SDS).

Results: Factor analysis of the individual delusions symptoms revealed three distinct and interpretable factors (58.4% of variance). Factor 1 (24.9%) was comprised by delusions of being controlled, thought insertion, and reading. It was significantly related to hallucinations (r=.459), severity of deficit syndrome (r=.381), avolition/apathy (r=.368) and attention (r=.275). Factor 2 (21.0%) was comprised by grandiose, religious, guilt/sin delusions, and delusions of reference and was significantly related to bizarre behavior (r=.437), avolition/apathy (r=.311), positive formal thought disorder (r=.269, p=) and alogia (r=.216). Factor 3 (12.4%) was comprised by persecutory delusions and was inversely correlated with alogia (r=.252).

Discussion: The results indicate that delusions should be considered heterogeneous clinical phenomena. Future research should focus on the links between specific delusions factors and putative neurobiological mechanisms.

NR56
Monday, May 3, 9:00 a.m.-10:30 a.m.
Symptom-Change Profile Over Time in the Treatment of Acute Schizophrenia

Megan Sherwood, M.D., Psychiatry Department, St. Paul's Hospital, 1081 Burrard Street, Vancouver, BC V6Z 1Y6, Canada; Allen E. Thornton, Ph.D., William G. Honer, M.D.
Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the pattern of improvement of schizophrenia symptoms over the first six weeks of acute exacerbation and demonstrate knowledge of hypotheses offering theoretical understanding of the nonlinear response of psychotic symptoms to atypical antipsychotic medication.

Summary:
Objective: The time course of symptom response in acute schizophrenia is unclear. We hypothesized that the time course would be non-linear.
Method: A meta-analysis was performed using randomized, controlled clinical trials of five atypical antipsychotics reported in nine electronic databases. We included acute exacerbation studies with multiple BPRS or PANSS data points, which served as the outcome measure. A mixed factorial repeated measures analysis of variance was used.
Results: Twenty-one published clinical trials were identified. Reduction in total symptoms from baseline to four weeks was associated with a linear term (F=23.4, p=0.002) but not a quadratic term (F=0.051, p=0.83). In contrast, from baseline to six weeks linear (F=76.5, p<0.001) and quadratic terms (F=87.2, p<0.001) were observed. Inclusion of LOCF data altered the results at four weeks, but not six weeks; completion rates had no effect on results.
Discussion: This meta-analysis confirms our hypothesis for six-week data. The profile of symptom change is one of linear symptom reduction until four weeks, becoming a quadratic response by six weeks. A curvilinear profile of schizophrenia symptom reduction has possible implications with respect to trial design and clinical decision making.

References:
1. Davis JM, Chen N, Glick ID: A meta-analysis of the efficacy of second-generation antipsychotics. Arch Gen Psychiatry 2003; 60:563-564

NR57    Monday, May 3, 9:00 a.m.-10:30 a.m.
Mentalizing in Patients With Schizophrenia Treated With Different Antipsychotics
Iolia Savina, M.A., Psychology Department, Queens University, 5950 Bathurst Street, Apt. #204, Toronto, ON M2R 1Y9, Canada; Richard J. Beninger, Ph.D.

Educational Objectives:
At the conclusion of this poster the participant will recognize the differential effects of typical antipsychotics or the atypicals olanzapine, clozapine and risperidone on mentalizing (theory of mind) in schizophrenic patients.

Summary:
Introduction: Theory of mind (ToM, or mentalizing) is the ability to attribute mental states to oneself and others and it has been found to be impaired in schizophrenia. Activations of the medial prefrontal cortex have been associated with performance on ToM tests. Typical and atypical antipsychotic medications differentially affect c-fos expression in this region.
Hypothesis: We hypothesized that ToM performance in schizophrenic individuals treated with different antipsychotic medications may differ.

Methods: Schizophrenic patients were assigned to groups according to their medication: a group receiving various typical drugs (n=23), Clozapine group (n=18), Olanzapine group (n=20), and Risperidone group (n=23). The Control group (n=24) consisted of healthy volunteers. ToM functioning was assessed with a picture-sequencing task, two second-order ToM stories, and a Faux-Pas test.
Results: The Olanzapine and Clozapine groups performed similarly to Controls on ToM tasks. The Typical and Risperidone groups performed worse than the other groups on ToM tasks.
Conclusions: Schizophrenic patients treated with different antipsychotic medications perform differentially on ToM tasks. This finding provides another clue to the mechanisms of therapeutic action of antipsychotics.

References:

NR58   Monday, May 3, 9:00 a.m.-10:30 a.m.
Divalproex and Atypical Antipsychotic Doses Supported by Abbott Laboratories
Jon C. Collins, Ph.D., Mental Health and Addiction Services, Oregon Department of Human Services, 500 Summer Street NE, PO Box 14250, Salem, OR 97301; Benton H. McFarland, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the relationship between concurrent use of divalproex and doses of atypical antipsychotic medication among Medicaid clients with schizophrenia.

Summary:
Background: Data from randomized trials suggest that divalproex may augment the impact of atypical antipsychotic medication in the treatment of people with schizophrenia. It was hypothesized that this effect might translate into lower doses of atypical antipsychotic medication when divalproex is taken concurrently.
Methods: Data came from electronic records for 5,647 Oregon Medicaid clients with schizophrenia diagnoses (56% male, average age 45).
Results: The average dose of divalproex was 1,394 milligrams per day. After adjustment for age, gender, and Global Assessment of Functioning scores, there was no difference in atypical antipsychotic dose between users with versus without concurrent divalproex. The average adjusted daily dose of atypical antipsychotic used concurrently with divalproex was 304 mg in chlorpromazine equivalents and the average adjusted dose of atypical antipsychotic used without divalproex was also 304 mg chlorpromazine equivalents. There was a suggestion that concurrent divalproex treatment was used preferentially for more severely impaired individuals.
Conclusions: There was no evidence that concurrent use of divalproex led to lower doses of atypical antipsychotic medication. Preferential use of concurrent divalproex for severely impaired individuals and modest doses of divalproex may make it difficult to identify the impact of divalproex on antipsychotic dosing.
References:


NR59  Monday, May 3, 9:00 a.m.-10:30 a.m.
The Doctor-Patient Relationship, Medication Adherence, and Schizophrenia

Alan D. Schlechter, Department of Psychiatry, Mount Sinai School of Medicine, 1 Gustave-Levy Place Box 1230, New York, NY 10029; Debra Roter, Ph.D., Adam M. Brickman, M.A., Eki Edwards, B.A., Jack Hirschowitz, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the importance of the doctor-patient relationship in patients with schizophrenia. The participant will see the need to tailor their interviewing technique to increase schizophrenic patient satisfaction and improve medication adherence.

Summary:

Objective: To assess preferences among patients with schizophrenia for patient centered versus task focused physician communication style.

Background: Medication adherence is strongly associated with patient satisfaction with their physician. This work extends the study of patient satisfaction to patients with schizophrenia, where lack of medication adherence often leads to relapse and hospitalization.

Method: Sixty patients with schizophrenia are being recruited from inpatient psychiatric units (n=30) and outpatient vocational services (n=30). A normal control comparison group is comprised of 30 demographically similar psychiatrically-healthy individuals. Participants view two ten-minute videos of a physician interviewing a standardized psychiatric patient. The physician uses two different interviewing techniques; one is more patient centered and the other more task focused, as determined by the Roter Interactive Analysis System for evaluating doctor-patient interactions. After viewing each video a questionnaire is given to assess his or her perception of what occurred during the video and preference for physician style.

Results: Preliminary data suggest that patients with schizophrenia prefer a partnership type relationship with their physicians. Final results comparing adherent and non-adherent patients with schizophrenia, and matched normal controls, are currently underway and will be presented.

Conclusion: The results of this study will help clinicians better understand the preferences among patients with schizophrenia for physician style. Physicians can then tailor their interviewing and clinical style to increase schizophrenic patient satisfaction, quality of care, and medication adherence.

References:


Summary:

Around 10% of patients with schizophrenia or schizoaffective disorder will die from suicide. This population based case-control study aims to identify risk factors for suicide among these patients. By linking the Patient Register with the Causes of Death Register, we identified the 100 last patients who committed suicide within 5 years from the first diagnosis of schizophrenia or schizoaffective disorder in Stockholm County. They had been admitted between June 1984 and December 2000. 100 controls were individually matched from the corresponding cohort of all the patients with a similar diagnosis (n=4000).

For the 4000 patients, the median age at diagnosis was 34 years (53, 6% male and 46, 4% female). For the 100 cases, the median age at diagnosis was 29.5 years (55 male and 45 female). 59 suicides occurred within one year from the diagnosis, 24 in the second year, while in the fifth year only two suicides occurred. The most frequent methods of suicide were poisoning (n=27) and hanging (n=23). For both cases and controls, the most common number of admissions before the first diagnosis was between two and five. Hospital records for the cases and controls are being collected for a detailed study of risk factors for suicide.

References:


NR62 Monday, May 3, 9:00 a.m.-10:30 a.m.

Social Disabilities Relate to Cognitive Functioning in Schizophrenia

Susana Ochoa-Guerre, M.S.C., Sant Joan de Deu - SSM, Dr. Pujades 42, St. Boi, Spain; Victoria Villalta-Gil, B.A., Miriam Vilaplana, M.S.C., Jaume Autonell, M.D., Susana Araya, M.D., Judith Usall, Ph.D., Joseph M. Haro, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to demonstrate that social disabilities are related to cognitive functioning.

Summary:

Objective: To analyze the relationship between neuropsychological functioning and social disabilities in outpatients with schizophrenia.

Method: A random sample of 60 outpatients with schizophrenia were evaluated with the Disability Assessment Scale-short version (DAS-sv) and a neuropsychological battery that included the Mini Mental Status Examination (MMSE), Stroop test, Trail Making Test A (TMTA) and B (TMTB), WAIS vocabulary, digits and simbol digits sub-scales, Wisconsin Card Sorting Test, FAS (verbal fluency), TAVEC (Spanish version of the California Verbal Learning Test) and the Continuous Performance Test (CPT).

Results: Association of DAS sub-scales and the cognitive was explained with multivariate linear regression. Word recognition and psychomotor speed explained the 29% of the variability of personal care dimension of the DAS-sv. Executive functioning explained the 33% of the variability of the occupational dimension. Psychomotor speed and verbal memory variables accounted for 49% of the variability of family dimension. And, psychomotor speed and verbal memory variables predicted the 46% of the variability of social functioning dimension.

Conclusions: People who show worse cognitive functioning in psychomotor speed and verbal memory have more social disabilities. These cognitive variables should be considered in further social and psychological treatment programs.

References:


NR63 Monday, May 3, 9:00 a.m.-10:30 a.m.

Neurodevelopment Relates to Clinical and Cognitive Variables in Schizophrenia

Montserrat Dolz, M.D., Department of Research, Sant Joan de Deu - SSM, Dr. Antoni Pujadas 42, St. Boi de Llo. 08830, Spain; Susana Ochoa-Guerre, M.S.C., Victoria Villalta-Gil, B.A., Miriam Vilaplana, M.S.C., Jorge Cervilla, Ph.D., Judith Usall, Ph.D., Joseph M. Haro, M.D.

Educational Objectives:

At the conclusion of this session, neurodevelopment relates to clinical and cognitive variables in schizophrenia.

Summary:

Objective: To relate developmental markers with clinical and neuropsychological variables in outpatients with schizophrenia.

Method: A random sample of 59 outpatients with schizophrenia (DSM IV criteria) were interviewed on a battery of neurodevelopment markers: neurological soft-signs (NES), obstetric complications (Lewis-Murray) and minor physical abnormalities (Waldrop). They also were administered a neuropsychological battery that includes Stroop test, Trail Making Test A-B, WAIS sub-scales, WCST, FAS (verbal fluency), TAVEC (verbal memory) and the CPT; a psychopathology scale (PANSS), and a extrapiramidal evaluation scale (SIMPSON). We also gathered information on socio-demographic data and illness evolution.

Results: Different linear regressions models were set between the Waldrop scale and PANSS sub-scales, SIMPSON, age of onset and cognitive variables. Using the stepwise method, the SIMPSON total score explained the 83% of the variability of the Waldrop scale and with the inclusion of the PANSS Negative sub-scale score was explained the 87% of that variability. NES scale correlates with SIMPSON (p < 0.001), PANSS Disorganized sub-scale (p < 0.005), Stroop (p<0.006) and WCST (p<0.001).

Conclusions: Minor physical abnormalities are more present in patients with more extrapiramidal and negative symptoms. Neurological soft-signs correlate with disorganized symptoms and with worse cognitive functioning.

References:


NR64 Monday, May 3, 9:00 a.m.-10:30 a.m.

Depression, Anxiety, and Quality of Life in Patients With Schizophrenia and Amenorrhea

Youn H. Kim, M.D., Psychiatry Department, Seoul National Hospital, 30-1 Junggok-3dong, Gwangjin-gu, Seoul 143-711, Korea; Kyu W. Youn, Ph.D., Mea K. Kim, M.D., Hye J. Lee, M.D.

Neurodevelopment Relates to Clinical and Cognitive Variables in Schizophrenia

Montserrat Dolz, M.D., Department of Research, Sant Joan de Deu - SSM, Dr. Antoni Pujadas 42, St. Boi de Llo. 08830, Spain; Susana Ochoa-Guerre, M.S.C., Victoria Villalta-Gil, B.A., Miriam Vilaplana, M.S.C., Jorge Cervilla, Ph.D., Judith Usall, Ph.D., Joseph M. Haro, M.D.

Educational Objectives:

At the conclusion of this session, neurodevelopment relates to clinical and cognitive variables in schizophrenia.

Summary:

Objective: To relate developmental markers with clinical and neuropsychological variables in outpatients with schizophrenia.

Method: A random sample of 59 outpatients with schizophrenia (DSM IV criteria) were interviewed on a battery of neurodevelopment markers: neurological soft-signs (NES), obstetric complications (Lewis-Murray) and minor physical abnormalities (Waldrop). They also were administered a neuropsychological battery that includes Stroop test, Trail Making Test A-B, WAIS sub-scales, WCST, FAS (verbal fluency), TAVEC (verbal memory) and the CPT; a psychopathology scale (PANSS), and a extrapiramidal evaluation scale (SIMPSON). We also gathered information on socio-demographic data and illness evolution.

Results: Different linear regressions models were set between the Waldrop scale and PANSS sub-scales, SIMPSON, age of onset and cognitive variables. Using the stepwise method, the SIMPSON total score explained the 83% of the variability of the Waldrop scale and with the inclusion of the PANSS Negative sub-scale score was explained the 87% of that variability. NES scale correlates with SIMPSON (p < 0.001), PANSS Disorganized sub-scale (p < 0.005), Stroop (p<0.006) and WCST (p<0.001).

Conclusions: Minor physical abnormalities are more present in patients with more extrapiramidal and negative symptoms. Neurological soft-signs correlate with disorganized symptoms and with worse cognitive functioning.

References:


Montserrat Dolz, M.D., Department of Research, Sant Joan de Deu - SSM, Dr. Antoni Pujadas 42, St. Boi de Llo. 08830, Spain; Susana Ochoa-Guerre, M.S.C., Victoria Villalta-Gil, B.A., Miriam Vilaplana, M.S.C., Jorge Cervilla, Ph.D., Judith Usall, Ph.D., Joseph M. Haro, M.D.

Educational Objectives:

At the conclusion of this session, neurodevelopment relates to clinical and cognitive variables in schizophrenia.

Summary:

Objective: To relate developmental markers with clinical and neuropsychological variables in outpatients with schizophrenia.

Method: A random sample of 59 outpatients with schizophrenia (DSM IV criteria) were interviewed on a battery of neurodevelopment markers: neurological soft-signs (NES), obstetric complications (Lewis-Murray) and minor physical abnormalities (Waldrop). They also were administered a neuropsychological battery that includes Stroop test, Trail Making Test A-B, WAIS sub-scales, WCST, FAS (verbal fluency), TAVEC (verbal memory) and the CPT; a psychopathology scale (PANSS), and a extrapiramidal evaluation scale (SIMPSON). We also gathered information on socio-demographic data and illness evolution.

Results: Different linear regressions models were set between the Waldrop scale and PANSS sub-scales, SIMPSON, age of onset and cognitive variables. Using the stepwise method, the SIMPSON total score explained the 83% of the variability of the Waldrop scale and with the inclusion of the PANSS Negative sub-scale score was explained the 87% of that variability. NES scale correlates with SIMPSON (p < 0.001), PANSS Disorganized sub-scale (p < 0.005), Stroop (p<0.006) and WCST (p<0.001).

Conclusions: Minor physical abnormalities are more present in patients with more extrapiramidal and negative symptoms. Neurological soft-signs correlate with disorganized symptoms and with worse cognitive functioning.

References:


Educational Objectives:

At the conclusion of this session, that female schizophrenic patients with atypical neuroleptic-induced amenorrhea are more likely to suffer from psychological distress such as depression and anxiety and lead a lower quality of life than those without amenorrhea do.

Summary:

Objective: Amenorrhea, one of the most common side effects of neuroleptics, has known to be associated with prolactin elevation. Hyperprolactinemia seriously affects mental health causing depression, anxiety or hostility, while affecting physical health as well, resulting in amenorrhea, galactorrhea or sexual dysfunction. The possible correlation between atypical neuroleptic-induced amenorrhea and depression, anxiety and quality of life is evaluated in a cross-sectional open study.

Method: During a five-month period, WHO quality of life-BREF (WHOQOL), Beck depression inventory (BDI) and State-trait anxiety inventory (STAI) were applied twice at two-month intervals; 30 patients with atypical neuroleptic-induced amenorrhea were compared with 30 patients without amenorrhea.

Result: Amenorrhea group had significantly higher scores in BDI and STAI-state while showing lower scores in the quality of life than control group. The total BDI and STAI-state scores were more negatively correlated with WHOQOL score in amenorrhea group.

Conclusion: Patients with atypical neuroleptic-induced amenorrhea rated themselves significantly more depressed and more anxious, leading a lower quality of life than control group. Clinicians should be more active in evaluating and treating the hyperprolactinemic side effects such as amenorrhea, galactorrhea, depression and anxiety.

References:


NR65  Monday, May 3, 9:00 a.m.-10:30 a.m.
Cognitive Functioning Predicts Psychopathological Dimensions in Schizophrenia

Victoria Villalta-Gil, B.A., RDH, Sant Joan de Deu - SSM, Dr. Antoni Pujadas 42, St. Boi de llobreg, AT 08830, Spain; Miriam Vilaplana, M.S.C., Susana Ochoa-Guerre, M.S.C., Montserrat Dolz, M.D., Jorge Cervilla, Ph.D., Matias Zamora, B.A., Josep M. Haro, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize variables of cognitive functioning relevant to explain the variability of psychopathological dimensions in a Spanish sample of schizophrenic patients

Summary:

Objective: To evaluate how cognitive functioning relates to psychopathology in patients with schizophrenia.

Method: Cross-sectional study with 84 Spanish outpatients fulfilling DSM-IV criteria for Schizophrenia, randomly selected. Patients were administered the Positive and Negative Symptom Scale (PANSS) and a neuropsychological battery that included: Mini Mental Status Examination (MMSE), Stroop test, Trail Making Test A and B, WAIS vocabulary, digits and symbol digits sub-

NR66  Monday, May 3, 9:00 a.m.-10:30 a.m.
Family Burden Relates to Clinical and Social Variables in Schizophrenia

Victoria Villalta-Gil, B.A., Department of Research, Sant Joan de Deu - SSM, Dr. Antoni Pujadas 42, St. Boi de Llo, AT 08830, Spain; Miriam Vilaplana, M.S.C., Susana Ochoa-Guerre, M.S.C., Judith Usall, Ph.D., Montserrat Dolz, M.D., Jaume Autonell, M.D., Joseph M. Haro, M.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to recognize social and clinical variables of patients with schizophrenia that have a direct impact on family burden.

Summary:

Objective: to study the burden of caregiver of patients with schizophrenia, and how it relates with patients' clinical and social variables.

Methods: We evaluated 147 caregivers of 231 randomly selected Spanish outpatients with schizophrenia (DSM-IV criteria). Objective and subjective burden was assessed with ECOSF-II (Assessment of Objective and Subjective Family Burden). Patients were assessed with The Global Assessment Functioning scale (GAF), the PANSS and the Disability Assessment Scale (DAS-SV).

Results: Caregivers had more objective burden in activities of daily life when the care receiver was a man (p<0.001). There was a positive correlation between DAS-SV total score and the objective and subjective burden (P<0.05-0.001) as well as between the psychopathological dimensions of the PANSS and the objective burden subscales (p < 0.05). We found negative correlation between GAF and some objective or subjective ECOSF following subscale: activities of daily life (p <0.05), caregivers daily activity impact (p < 0.001) and caregiver concerns (p < 0.05). Subjective burden reported by caregivers was much higher than the objective burden.

Conclusions: Subjective burden is higher than objective burden in caregivers of patients with schizophrenia. Higher disability, worse global functioning and more psychopathological severity were associated with most family burden.
References:


NR67 Monday, May 3, 9:00 a.m.-10:30 a.m.
Study of Risk Factors for Medication Nonadherence In Schizophrenia
Amit Razdan, M.D., Department of Psychiatry, Virginia Treatment Center for Children, 515 N. 10th Street, PO Box 980489, Richmond, VA 23228; Kavir Saxena, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to understand the issue of medication non-adherence in patients with schizophrenia. The participant should be able to evaluate risk factors for medication non-adherence and be able to identify patients with higher risk of non-adherence. Possible intervention strategies will also be discussed.

Summary:
Introduction: Despite the rapid advances in psychopharmacological research leading to new antipsychotics, the enthusiasm is dampened by the continuing medication nonadherence in patients with schizophrenia. The present study was done to evaluate risk factors for medication nonadherence in patients with schizophrenia primarily in an outpatient setting.

Methods: Forty-five medication adherent and forty-five medication nonadherent patients with schizophrenia were taken up for the study. The following tools were applied: (a) Semi-structured proforma including identification data, psychiatric history, physical examination, mental status examination, and socio-demographic variables. (b) Diagnosis was confirmed using ICD-10 diagnostic criteria for research (DCR) 1993 for schizophrenia. (c) Rating of medication influences scale (ROMI-Weiden P.J., Rapkin B, and Mott T et al: Schizophr Bull. 1994, 20:297-310). (d) Positive and negative symptoms scale (PANSS). (e) Global assessment of functioning scale (GAF). (f) UKU side effect rating scale (Lingjaerde O et al 1997).

Results: Patient related risk factors for nonadherence: poor insight, negative attitude towards medications, negative subjective response to medication, previous nonadherence, substance abuse and shorter duration of illness. No significant association of age, gender, marital status, or educational level.

Medication-related risk factors for nonadherence: Severity of side effects, use of typical medications (vs. atypical) medications, and medication regimen complexity. Higher antipsychotic dose, and use of oral versus depot medication did not consistently correlate with degree of nonadherence.

Environmental risk factors for nonadherence: Poor therapeutic alliance, and inadequate discharge planning/poor aftercare.

Conclusions: Evaluation of risk factors for medication nonadherence may be recommended in every patient with schizophrenia to improve treatment outcome and decrease the risk of relapse. I attest that I prepared this abstract, all funding is acknowledged in this abstract, and I will present the poster on site.

References:
Methods: 50 outpatients with pathological gambling treated in a clinical practice were assessed by chart review. Standard scales were used to rate subjects. Subjects who dropped out of treatment were contacted to determine reasons for discontinuation of treatment.

Results: The mean duration of follow-up = 360 days. 24 (48%) subjects discontinued treatment, including 14 (27%) of those subjects who were treatment responders. Of those who discontinued treatment, 42% reported missing the thrill of gambling and 21% reported feeling certain that they could win and relieve financial burdens. Predictors of treatment continuation: responding to treatment within 8 weeks (odds ratio = 6.00; 95% CI: 1.13-32.00; p = 0.04) and having a supportive environment (odds ratio = 22.99; 95% CI: 5.04-104.76; p<0.001).

Conclusions: A large percentage of patients with pathological gambling discontinue treatment.

References:

NR70 Monday, May 3, 9:00 a.m.-10:30 a.m.
Dropping Out in a Spanish Outpatient Care Center
Carlos Carmona, M.D., Department of Research, Sant Joan de Deu - SSM, Dr Antoni Pujades 42, Sant Boi 08830, Spain; Jaume Autonell, M.D., Josep M. Haro, M.D., Francesc Perez-Arnau, Ph.D., Ana Fernandez, B.A., Inmaculada Luque

Educational Objectives:
At the conclusion of this session, participants attending to a mental health service show high rates of “drop-outs”. Age and diagnosis seem to be associated with dropout.

Summary:
Objective: to examine differences between patients who leave and do not leave treatment in Sant Joan de Deu Serveis de Salut Mental (SJD-SSM) outpatient services.
Method: All patients who contacted with SJD-SSM for the first time, between January and December 2001, were followed-up until October 2003. Data was collected using the information provided by the computerized clinical chart of SJD-SSM. From this database, socio-demographics (sex and age), clinical data (Global Assessment Functioning (GAF)) and DSM-IV diagnostic criteria were extracted. Patients who failed to return after the last outpatient programmed visit were regarded as “drop-outs”. Patients attending until discharge, referred, that moved outside the catchment area or that died during the follow-up were not considered as drop-outs.

Results: From the 3,435 patients in ongoing treatment, 49.9% had droped-out at follow-up. Drop-outs were younger, more likely to have a diagnosis of anxiety disorder or eating disorder, and less likely to have schizophrenia or mood disorders. No statistical differences were found on GAF or sex.

Conclusions: A high rate of drop-outs is observed in subjects attending to a mental health care, service. More effective interventions are needed in order to increase the proportion of patients completing adequate courses of treatment.

References:
Thornton, Ph.D., Edward Gottheil, M.D., Michael J. Vergare, M.D., Paolo Mannelli, M.D., Heather W. Murray, M.D.

**Educational Objectives:**
At the conclusion of this session, the participant should be able to recognize the potential mediators for depression as a predictor of treatment outcome in cocaine dependent patients.

**Summary:**

**Objectives:** To identify cognitive/behavioral factors that mediate the association of depression with treatment outcome in cocaine-dependent patients.

**Methods:** 76 cocaine-dependent patients were assessed with the Beck Depression Inventory (BDI), Learned Helplessness Scale, Treatment Readiness Questionnaire, and Coping Scales. Outcome was assessed by urine drug screens, Addiction Severity Index (ASI), and counselor/patient rating.

**Results:** BDI score of > 16 was associated with greater Learned Helplessness, higher ASI composite score-drug (pretreatment), and lower Treatment Readiness (specifically: effect of drug use on other areas; and the beliefs that the drug/ alcohol problems were more serious, that the patient will relapse during treatment, and that emotional/psychosocial problems might interfere with treatment). On Coping Scales, it was associated with less positive reinterpretation, more behavioral disengagement, and greater alcohol/drug use to treat feelings. Being depressed predicted several (though not all) of the outcome measures. All these findings were statistically significant even when controlling for the first urine drug screen being negative, except Learned Helplessness (p=0.067).

**Discussion:** It is important that the cognitive and behavioral features identified as associated with depression and as affecting treatment outcome be specifically addressed in designing new interventions.

**References:**

**NR73 Monday, May 3, 9:00 a.m.-10:30 a.m.**

**Quetiapine Inhibits Cell Growth, Decreases GFAP, and Increases GDNF in C6 Glioma Cells Supported by AstraZeneca Pharmaceuticals**

Xin-Min Li, M.D., Department of Neuropsychiatry, University of Saskatchewan, 103 Wiggins Road/A14 Med Res Bldg, Saskatoon, SK S7N 5E4, Canada; Zhong-Jun Shao, M.D., Lillian E. Dyck, Ph.D.

**Educational Objectives:**
At the conclusion of this presentation, the participant should be able to describe the relationships between brain injury, astrogliosis, and subsequent scar formation, and summarize the protective effects of quetiapine in reducing cell number. GFAP expression, and GDNF release in a cell line model of astrogliosis.

**Summary:**

**Objective:** To examine the effects of quetiapine, clozapine, and haloperidol on cell growth, cell mortality, glial fibrillary acidic protein (GFAP) expression, and glial cell derived-neurotrophic factor (GDNF) release in rat C6 glial cells.

**Methods:** Cell number was assessed using a WST-8 kit; trypan blue exclusion measured cell death, and phase contrast microscopy determined cell morphology. Western blot detected GFAP expression; area and density were analyzed using Image-Pro Plus software. GDNF levels were assessed by enzyme-linked immunosorbant assay. Statistical comparisons were done by one-way analysis of variance followed by Tukey’s HSD test.

**Results:** C6 cell number after culturing for 72 hours was decreased with 25 and 50 |μ|M quetiapine and clozapine, but not haloperidol. None of the antipsychotics increased cell mortality. Quetiapine decreased GFAP protein levels significantly after culturing for 48 hours, whereas clozapine and haloperidol did not. GDNF release was increased with 10, 25, and 50 |μ|M of quetiapine and clozapine, and 25 and 50 |μ|M of haloperidol.

**Conclusion:** Quetiapine may be useful for regulating astrogliosis that occurs after brain injury and in some neurodegenerative diseases.

**References:**

**NR74 Monday, May 3, 9:00 a.m.-10:30 a.m.**

**Prolactin, Severity of Drug Use, and Treatment Outcome in Cocaine Dependence**

Adam C. Frey, B.A., Psychiatry Department, Thomas Jefferson University, 833 Chestnut Street, Suite 210 E, Philadelphia, PA 19107; Ashwin A. Patkar, M.D., Paolo Mannelli, M.D., Michael J. Vergare, M.D., Marja Mattila-Evenden, M.D., Heather W. Murray, M.S., Wade H. Berrettini, M.D.

**Educational Objectives:**
At the conclusion of this session, the participant should be able to recognize the relationship of biological markers to severity of illness and treatment outcome in substance abuse.

**Summary:**

**Objective:** Alteration in serum prolactin (PRL) levels may reflect changes in central dopamine activity that modulate the behavioral effects of cocaine. We investigated the differences in serum prolactin (PRL) levels in cocaine-dependent (CD) subjects and controls, and the relationship of PRL levels to severity of drug use and treatment outcome in CD subjects.

**Method:** Serum PRL concentrations were assayed in 141 African-American (AA) CD patients attending an outpatient treatment program and 60 AA controls. Severity of drug use was assessed using the Addiction Severity Index (ASI). Measures of abstinence and retention during 12 weeks of treatment and at 6 months follow-up were employed as outcome variables.

**Results:** Basal PRL (ng/ml) in CD patients (9.28 ± 4.13) was significantly higher than in controls (7.33 ± 2.94) (t = 3.77, p<0.01). Furthermore, PRL was positively correlated with ASI-drug (r = 0.38, p < 0.01), ASI-alcohol (r = 0.19, p < 0.05), and ASI-psychological (r = 0.25, p < 0.01) composite scores, and with the quantity of cocaine use (r = 0.18, p < 0.05). However, PRL levels were not significantly associated with the number of negative urine screens, days in treatment, number of sessions attended, dropout rate, or changes in ASI scores during treatment and at follow-up.

**Conclusion:** Although certain measures of drug addiction severity may influence PRL levels, it does not appear that PRL is associated with outcome measures in cocaine dependence.

**References:**
1. Patkar AA, Hill KP, Sterling RC, Gottheil E, Berrettini WH, Weinstein SP: Serum prolactin and response to treatment...


NR75 Monday, May 3, 9:00 a.m.-10:30 a.m.
Quantification of Myo-inositol and Other Metabolites in Patients With Bipolar Disorder and Lithium Treatment Determined by Frontal H-Magnetic Resonance Spectroscopy
Theresa Lahousen, M.D., Psychiatry Department, University of Graz, Auenbruggerplatz 31, Graz 8036, Austria; Karin Hasiba, M.D., Peter Hofmann, M.D., Stefan Ropele, Ph.D., Christian Enzinger, M.D., Franz Fazekas, M.D., Peter Kapeller, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize that these findings highlight the need for caution in the interpretation of in vivo MRS studies using ratio data.

Summary:

Introduction: One of the most widely accepted hypotheses for the mechanism of action of lithium which is able to explain both its clinical effectiveness and clinical specificity is the "inositol depletion" hypothesis. A number of in vivo 1H MRS studies have used a ratio method of data expression where the Cr+PCr peak acts as a reference against which all compounds of interest are compared. Several findings suggest that future in vivo 1H MRS research of lithium-treated patients must employ quantification methods versus ratio data expression if the results obtained are to be reliable.

Methods: Lithium's effects on in vivo brain myo-inositol levels and other metabolites were investigated in 9 patients with bipolar disorder (f/m=1/8; mean age: 45 years) following lithium treatment which was adjusted to obtain a therapeutic plasma level (0,6-1,1meq/liter) and 9 healthy volunteers (f/m=1/8; mean age: 44 years). Sagittal T2 (TR/TE: 2700/120) and transversal T1 (TR/TE: 460/14) scans were used as localizer. Quantitative single-voxel 1H MRS examinations were performed by using 1,5-T clinical scanner and a short echo single voxel (TR/TE: 3000/30) placed in brain anterior cingulate cortex (3x1,5x1,5). The user independent method LC Model served to quantify the concentrations of N-acetyl-aspartate, choline, creatine and myo-inositol. The reliability of measure data was controlled for by periodic calibration of the MR scanner against standard solutions of known concentration for spectroscopy.

Results: Patients who received lithium showed a significant decrease in the concentration of myo-inositol (4,615 versus 6,592; p<0,05) and further a significant reduction of N-acetyl-aspartate concentration in patients with bipolar disorder (7,996 versus 8,978; p<0,05). There was no difference of creatine and choline between the both groups.

Conclusion: As predicted, lithium-treated patients exhibited a significant decrease in myo-inositol concentration. In the present study chronic lithium caused N-acetyl-aspartate concentrations to significantly decrease in human brain. These results suggest that caution must be exercised when interpreting decreases in N-acetyl-aspartate as cell death when the possibility exists that neurons can have varying levels of N-acetyl-aspartate caused by an inherent dysfunction or the presence of drugs like lithium. Further research is required to identify the mechanism by which neuronal N-acetyl-aspartate is decreasing in the presence of lithium.

References:

NR76 Monday, May 3, 9:00 a.m.-10:30 a.m.
Regulation of GSK-3 Mediated Signaling Pathway by Clozapine in SH-SY5Y Cells
Yong-Sik Kim, M.D., Department of Neuropsychiatry, Seoul National Hospital, 28 Yongdongdong Gwangmyeong, Seoul 110-744, South Korea; Lee Kyuyoung, M.D., Seo Myoungsuk, M.S., Roh Myoungsun, M.D., Kim Yeni, M.D., Kang Unggu, M.D.

Educational Objectives:
At the conclusion of this session, clozapine may have neurotrophic effect and enhance cell survival through the regulation of Wnt signaling.

Summary:

Some psychotropic drugs such as lithium and valproate has proved to regulate GSK-3β by phosphorylation of Ser-9 resulting inactivation, GSK-3β is the key component of Wnt and P13K-Akt signaling pathways. Clozapine is one of psychotropic drugs shown to have neurotrophic effect. In this study we investigated the effect of clozapine on the activity of GSK-3β and its upstream and downstream molecules in SH-SY5Y human neuroblastoma cells. SH-SY5Y cells were exposed to 10 μM clozapine(0444, Tocris) and incubated at 37 °C. Here we show that clozapine activates both Akt-mediated and Dvl-mediated phosphorylation of GSK-3β through phosphorylation at Ser-9, and increased total cellular and intranuclear level of β-catenin in SH-SY5Y cells. At the level of clozapine 10 μM there was no increased in the phosphorylation of ERK1/2, another potential upstream kinase of GSK-3β. Since the specific inhibitor of P13K-Akt pathway was available, we pretreated the cells with LY294002 (20 μM) and then with clozapine. As expected, LY294002 pretreatment prevented the phosphorylation of Akt. However, the phosphorylation of GSK-3β was not effected by LY294002 pretreatment. These results suggest that clozapine regulate the phosphorylation of GSK3-β and subsequent nuclear translocation of β-catenin through Wnt-signal pathways involving Dvl in its upstream but not through P13K-Akt pathways in SH-SY5Y cells. In a physiological sense, clozapine may have neurotrophic effect and enhance cell survival through the regulation of Wnt signaling.

References:

NR77 Monday, May 3, 9:00 a.m.-10:30 a.m.
THC Effects on Virtual Navigation in Humans
Robert S. Astur, Ph.D., Hartford Hospital, Olin NRC/NIH, 200 Retreat Avenue, Hartford, CT 06106; Danielle Abi-Saab, Ph.D., Lia Donaghue, M.A., Edward Perry, M.D., D. Cyril D'Souza, M.D.
Educational Objectives:

At the conclusion of this session, the participant should be able to appreciate how cannabinoids affect hippocampus functioning in rodents and humans. Additionally, the participant should be able to understand how dose-response and memory factors determine the extent of hippocampus impairment observed following cannabinoid administration.

Summary:

Objective: Administration of tetrahydrocannabinol (THC) results in spatial memory impairments in rodents similar to hippocampal lesion impairments. The aim of this study was to examine whether THC diminishes spatial memory in the virtual Morris water task, a task shown to be sensitive to hippocampus damage. We observe that all participants show normal spatial learning.

Method: Nine healthy subjects without any psychiatric illness including current or lifetime diagnosis of cannabis abuse/dependence were included. Participants were tested on the virtual Morris water task with the pool placed in one of four rooms.

Results: All participants show normal spatial learning. If we examine the most critical test session of THC with no Naltrexone, we observe that all participants show normal spatial learning. During the probe trial of this session, in which the platform is removed from the pool, participants spend 66% of their swim distance in training quadrant of the pool, indicating that spatial memory was intact.

Conclusion: THC does not impair spatial memory in the virtual Morris water task. Dose-response dependency and working memory vs. reference memory contributions to these results are discussed.

References:


NR79 Monday, May 3, 9:00 a.m.-10:30 a.m.
The Relation of Global Cognitive Processing Indices to Cortical and Subcortical Volumes
Melanie H. de Luna, Psychiatry Department, UCSF/UC Irvine, 4914 Verano Place, Irvine, CA 92612; Sophia Vinogradov, M.D., John Poole, Ph.D., Raymond Deicken, M.D.

Educational Objectives:

At the conclusion of this session, the participant will be able to recognize key relationships between certain global cognitive deficits in schizophrenia and measures of cortical and subcortical brain volumes.

Summary:

Background: Schizophrenic subjects show multiple cognitive deficits, which prior research has attempted to relate to regional brain volumes. In this study, we investigated the relationship of cortical and subcortical brain volumes to global indices of cognitive ability and information processing efficiency, in a sample of schizophrenic outpatients and healthy controls.

Methods: Quantitative high-resolution magnetic resonance images (MRI) were collected from 46 schizophrenic subjects and 22 healthy controls, to measure intracranial volume (ICV), total cortical and cortical gray matter, total white matter, and total volumes of the hippocampus, thalamus, caudate, and putamen. Subjects also completed a comprehensive neuropsychological battery, which provided global indices of central and peripheral cognitive processing efficiency, speed, and accuracy (derived by Brinley-regression analysis).

Results: In the schizophrenic group, total cortical gray matter was significantly and positively correlated with central cognitive processing efficiency (with equal contributions to both speed and accuracy of processing). Also in patients, overall processing speed but not accuracy was correlated with total ICV, mainly due to an association with total white. Schizophrenic subjects' hippocampal, thalamic, and striatal volumes were unrelated to these indices of global cognitive processing efficiency. In controls, only thalamic volume correlated positively with overall processing efficiency.

Conclusions: In schizophrenia, reductions of overall cognitive processing efficiency (both speed and accuracy) are related to...
lower cortical gray matter volumes. Reductions in speed of responses (but not accuracy) are related to white matter decrements. These relationships are different from those observed in normal controls. These findings indicate that impaired cognitive processing in schizophrenia is related to pathological processes affecting cortical gray and white matter, and that these processes are not just extreme versions of the normal-range variations of ability in healthy individuals.

**References:**


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**NR80**

**Monday, May 3, 9:00 a.m.-10:30 a.m.**

**Gender Differences in Cerebral Metabolism During Sustained Sadness**

Ralph Fenn, M.D., Psychiatry Department, Stanford University, 401 Quarry Road, Room 2115, Stanford, CA 94305-5723; Po W. Wang, M.D., Nadia Sachs, M.D., Cecylia Nowakowska, M.D., Nathan F. Dieckmann, B.A., Terence A. Ketter, M.D.

**Educational Objectives:**

At the conclusion of this session, the participant should be able to recognize that healthy women compared to men have more extensive paralimbic cerebral metabolism decreases with sustained sadness induction.

**Summary:**

**Objective:** To assess gender differences in cerebral metabolism (CMRglu) with sustained sadness.

**Method:** We studied CMRglu in 12 healthy women (age 33.8±12.9) and 12 healthy men (35.3±12.9) with fluorine-18 deoxyglucose (FDG) and positron emission tomography (PET) at rest (passive introspection for 30 minutes) and during a sustained sadness task (recalling sad memories for 30 minutes).

**Results:** Women compared to men had 35% larger increases in PANAS sadness subscale scores (11.5±3.3 vs. 8.5±2.6, p<0.03) and 12-fold more widespread CMRglu decreases (7528 vs. 615 voxels with p<0.01 threshold). Although CMRglu decreases were far more widespread in women, the anterior paralimbic network involved was similar across genders (left more than right insula, bilateral medial frontal gyrus/anterior cingulate, caudate and thalamus).

**Conclusion:** These data suggest that female compared to male healthy volunteers are moderately (35%) more effective at self-induced sustained sadness, and this is accompanied by dramatically (12-fold) more widespread decreases in anterior paralimbic activity, in a network overlapping that implicated in major depression.

**References:**


Methods: From a website that provides names of prominent musicians with AP we identified 20 musical figures with well documented AP. We assessed the available biographical material on these 20 musicians for evidence of autism spectrum disorders and other major psychiatric disorders.

Results: Four of the 20 prominent musicians with AP met the DSM IV criteria for Asperger's Disorder and two met most of the criteria. The estimated prevalence of Asperger’s Disorder in the general population is 2-6 per 1000. The prevalence of Asperger’s in our sample is more than 30 times that in the general population (4/20 vs 6/1000, $X^2 = 76.02, p<.001$). No other psychiatric conditions had a prevalence in our sample different from that in the general population.

Conclusions: Notwithstanding the limitations on the diagnostic inferences one can draw from biographical material, our results provide further evidence for an association between AP and autism spectrum disorders. They also underscore the fact that people with severe impairments in their ability to communicate and socialize are capable of extraordinary occupational and artistic achievement.

References:

NR83 WITHDRAWN

NR84 Monday, May 3, 9:00 a.m.-10:30 a.m.
Placental Passage of Lithium and Lamotrigine

Aquila J. Beach, B.A., Psychiatry Department, Emory University, 1365 Clifton Road NE Suite 6100, Atlanta, GA 30322; Page Pennell, M.D., D. Jeffrey Newport, M.D., James C. Ritchie, Ph.D., Zachary N. Stowe, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to be aware of the preliminary data on the extent of placental passage of lithium and lamotrigine.

Summary:
Managing Bipolar Disorder during pregnancy represents a complex clinical decision. Based on available reproductive safety data, there are limited pharmacological maintenance alternatives for Bipolar Disorder during pregnancy. Similarly, there are no established therapeutic monitoring guidelines of these medications during pregnancy (e.g. dose adjustment in the prevention of symptoms and following childbirth). Recent studies from our group have demonstrated significant alterations in lamotrigine clearance during pregnancy consistent with increased glucuronidation activity during pregnancy (Pennell 2003). Another aspect to consider, in guideline development is the extent of fetal and neonatal exposure with lithium and lamotrigine. A total of 11 women treated with lithium (mean dose 937±492.6 mg/day) and 3 women treated with lamotrigine (mean dose 525±357.1 mg/day) were included in the present study. Maternal sera and umbilical cord blood pairs were collected from women at time of delivery. Placental passage of lithium is 1.0±0.16 indicating complete placental passage. Analysis of 1 lithium pair and 6 additional lamotrigine pairs during pregnancy and collection of obstetrical records are pending at time of submission. The impact of pregnancy on maternal serum concentrations, umbilical cord concentrations (e.g. fetal exposure) will be presented. Data will be discussed on the development of therapeutic monitoring guidelines.

References:

NR85 Monday, May 3, 9:00 a.m.-10:30 a.m.
Attachment Stability, Paternal Alcoholism, and Infant Behavior Problems

Jennifer R. Scarozza, M.D., Psychiatry Department, SUNY at Buffalo, 888 Delaware Avenue, Buffalo, NY 14092; Kenneth E. Leonard, Ph.D., Rina D. Eiden, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize risk factors for infant behavior problems including paternal alcoholism, unstable attachment with fathers, and stable insecure attachment with mothers.

Summary:
Objective: Infant attachment security has been related to later behavior problems. However, attachment security displays a moderate degree of change over time. This study explores attachment stability over time and its implications for behavior problems among children of alcoholics and controls.

Method: This study followed children whose attachment security was assessed with the Ainsworth Strange Situation paradigm at 12 and 18 months of age. Parents completed the Child Behavior Checklist at 18, 24 and 36 months of age to assess internalizing and externalizing behavior problems.

Results: Mother and father attachment was classified as stable secure, stable insecure, or unstable. These attachment groups did not predict externalizing behaviors, but paternal alcohol problem was significantly correlated with externalizing behaviors. Stable insecure attachment with mothers was related to a high level of internalizing problems for boys, but not for girls. Children characterized by unstable attachments with fathers also had higher internalizing problems.

Conclusion: The results suggest that paternal alcoholism had a more pronounced impact on externalizing problems than attachment. However, internalizing problems were more strongly tied to stable insecure attachment with mothers and unstable attachment with fathers.

References:

NR86 Monday, May 3, 9:00 a.m.-10:30 a.m.
Comparison of Agitation Episodes: 1993 and 2003
Supported by Janssen Pharmaceutica and Research Foundation

David M. Margulies, M.D., Department of Psychiatry, Stony Brook University, Putnam Hall, South Campus, Stony Brook,
NY 11794-8790; Gabrielle Carlson, M.D., Zinoviy Gutovich, M.D.

Educational Objectives:
At the conclusion of this session, the audience will learn about the changes in rates of seclusion and restraint and impact of newer medications on agitation requiring intervention in psychiatically hospitalized children.

Summary:
Purpose: To examine frequency, duration and impact of newer medications on agitation requiring intervention in psychiatically hospitalized children.

Method: Consecutively admitted children (with severe aggression) from April-December/2003 (n=63 admissions to date) were compared with 257 admissions from 1987-1993 regarding number, timing and medication use. Controlling for aggression, recently hospitalized children had fewer episodes requiring seclusion or medication intervention (65 vs 53% had any such episode; 20.5 Vs 5.3% had 8 or more episodes). Controlling for the drop in length of stay, episodes of agitation have dropped from 0.11/day to 0.03/day. 10 years ago, stimulants were prescribed for 76% of aggressive patients needing restraint; antidepresants for 36%, mood stabilizers for 17%, clonidine for 5% and conventional antipsychotics for 12.7%. In 2003, percent use, respectively, is 43%, 47%, 46%, 10% and 73% for atypical antipsychotics. Duration of episodes has not changed. Up to 1993, 20% of children had episodes of 15 minutes or less, 18% 30 minutes, 12% 45 minutes, and 50% for an hour or longer. In 2003, the frequency is 24%, 14%, 7% and 55%.

Conclusion: Current medication strategies have reduced the frequency of episodes of agitation for many children, at least within the structure of a well run inpatient unit. The duration of episodes is unchanged.

References:

NR87  Monday, May 3, 9:00 a.m.-10:30 a.m.
Internet-Based Information Resources in Reproductive Psychiatry: The Massachusetts General Hospital Experience
Amanda K. Zurick, B.A., Psychiatry Department, Mass. General Hospital, 15 Parkman Street, WACC 815, Boston, MA 02114; Ruta M. Nonacs, M.D., Adele C. Vigueru, M.D., Claudio N. Soares, M.D., Hadine Joffe, M.D., Lee S. Cohen, M.D.

Educational Objectives:
At the conclusion of this session the participant should understand that the Internet can be an effective and prompt way to disseminate information regarding research findings and their implications.

Summary:
Objective and Background: To describe the application of an internet-based information resource in reproductive psychiatry. Despite recent advances in reproductive psychiatry, many critical questions that can inform clinical care remain unanswered. In addition, as new research findings are published, there is frequently a period of time during which there is ambiguity regarding the implications of these findings. In recent years, the Internet has been used as a way of quickly disseminating information including scientific findings; however, several studies have demonstrated that a significant percentage of medical information available through the Internet is incorrect.

Method: The Center for Women's Mental Health at The Massachusetts General Hospital established an internet-based information resource center approximately 24 months ago. The goal of the Center is to provide accurate information to patients and clinicians across topics in women's mental health. Site statistics describing the number of visitors to the site, keywords searched, duration of visits and distribution of page views by area is evaluated in an ongoing way.

Results: The website (www.womensmentalhealth.org) receives approximately 15,000 visits per month. Page views by area of greatest interest include psychotropic drug use during pregnancy, menopausal mood disturbance and premenstrual dysphoric disorder. A relationship appears to exist between timing of searches and periods during which new research findings are presented in scientific literature or lay media.

Conclusions: Internet-driven information resources may be of particular help in the area of women's mental health. Accurate and timely presentation of information allows for thoughtful treatment decisions.

References:

NR88 Monday, May 3, 9:00 a.m.-10:30 a.m.
Implementation of the Computerized, Neurocognitive Function Tests for Children With ADHD
Daiseg Bai, Ph.D., Psychiatry Department, Yeunam University Hospital, Daemyung Dong Namgu, Daegu 705-717, South Korea; Jongburn Lee, M.D., Eunjung Jung, M.D., Shinho Song, M.D.

Educational Objectives:
At the conclusion of this session, the computerization for assessment of ADHD was more effective than conventional neuropsychological tests.

Summary:
The objective in this study was to verify the effect of computerization of the ADHD assessment. K-ABC, K-PIC, behavioral symptom checklists and CNFT were performed on the 120 normal children who had over the average of intelligence and passed the rule out criteria. To verify the effect of computerization of ADHD assessment, same tests were performed to the 31 ADHD children, and the 16 non ADHD children. Comparing the result among the three groups, most of variables had significant difference between the normal children and others. In discriminate analysis, the computerized system had higher values than the conventional neuropsychological test in specificity(99.0%), sensitivity to the ADHD(55.6%) and non ADHD(66.7%), and accuracy(89.5%). In conclusion, this study confirms that the computerization for assessment of ADHD was more effective than conventional neuropsychological tests. However, further investigation will need for the discrimination from the other disease. It is recommended web based multi-subject testing system for the one expert.

References:
NR89  Monday, May 3, 9:00 a.m.-10:30 a.m.
The Neuropsychological Characteristics of the Elementary School-Aged Child by the Computerized, Neurocognitive Function Test
Daiseg Bai, Ph.D., Psychiatry Department, Yeunam University Hospital, Daemyung Dong Namgu, Daegu 705-717, South Korea; Jongboun Lee, M.D., Eunjung Jung, M.D., Shinho Song, M.D.

Educational Objectives:
At the conclusion of this session, the computerized neurocognitive function test devised for adult can be used of assessing child neuropsychological characteristics

Summary:
This study is to examine the neuropsychological and developmental characteristics of the computerized neurocognitive function test(CNFT) among normal children in elementary school. K-ABC, K-PIC, and CNFT were performed to the 120 body of normal children(10 of each male and female) from June, 2002 to January, 2003. Those children had over the average of intelligence and passed the rule out criteria. As a result, although 21.1% were excluded from of total participants, the children that passed the rule out criteria had over the average of intelligence and not differ in the intelligence level among the graders. CNFT results among the graders, almost of variables had significant difference among the graders and especially between the 1st(6 year) to 2nd(7 year) and the 5th(10 year) to 6th(11 year) graders. In the attention tests, as rising the graders, the performance of tests were improved. In the short-term memory tests, the difference between forward and backward tests were same as the previous research result. The verbal auditory learning test composed of recall task and visual figure memory test composed of recognition task were same as the previous research result using the individual power or achievement test and also as rising the graders, the performance of those tests were improved. The higher cognitive function tests had the same results with other tests. The CNFT devised for adult can be used of assessing child neurocognitive characteristics and for the this objective, strict sampling criteria, control of the intelligence and psychopathology were needed.

References:

NR90  Monday, May 3, 9:00 a.m.-10:30 a.m.
Injectable Ziprasidone for Severely Agitated Adolescents
Steven G. Klotz, M.D., Department of Psychiatry, SUNY Stony Brook, Health Science Center T-10, Room 020, Stony Brook, NY 11794-8101; Horacio Preval, M.D., Robert Southard, N.P., Andrew J. Francis, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to discuss the efficacy and tolerability of IM ziprasidone in severely agitated adolescents in the ER setting

Summary:
Objective: Injectable atypical neuroleptics may supplant benzodiazepine and/or butyrophenone alternatives. Published trials of intramuscular [IM] ziprasidone excluded agitated children and adolescents who require IM sedation.
Method: During a naturalistic ER study of IM sedatives, we administered 20 mg IM ziprasidone to 6 severely agitated adolescents. For 5 of these, BARS scale agitation scores [min=1, max=7] were obtained before and after IM medication. Clinical outcome was summarized for all 6.

Results: The sample included 3 males (age 14-17) and 3 females (age 13-14) with varied psychiatric diagnoses. One male had cannabis detected on toxicologic screening. Mean ±SE baseline BARS scores of 7.0±0.0 decreased to 4.0±0.8 by 30 min (P<.05), and to 3.0±0.8 by 60 min (P<.01) post-IM ziprasidone. (These scores coincide with those of agitated adult patients receiving IM ziprasidone.) No adverse clinical effects were noted. EKGs obtained from two adolescents post-IM ziprasidone were normal (QTc 387-423 ms). Four patients required transient (<35 min) physical restraints. Agitated episodes resolved uneventfully for all patients.

Conclusion: IM ziprasidone was effective and well-tolerated in severely agitated adolescents. It offered prompt sedation similar to that shown for adults. Its use may lead to reduced use of physical restraints.

References:

NR91  Monday, May 3, 9:00 a.m.-10:30 a.m.
Prescribing to Patients Discharged From a Psychiatric Emergency Service
Carrie L. Ernst, M.D., Psychiatry Department, Cambridge Hospital, 91 Trowbridge Street, Apt. 22, Cambridge, MA 02138; Suzanne Bird, M.D., Joseph F. Goldberg, M.D., S. Nassir Ghaemi, M.D.

Educational Objectives:
At the conclusion of this session, the participants will understand the issues relating to prescribing decisions in the psychiatric emergency setting and their implications for subsequent aftercare.

Summary:
Objective: There has been considerable debate about the value of beginning “definitive pharmacotherapy” in the psychiatric emergency setting. Few empirical studies, however, have addressed this issue. We evaluated the extent to which medications were prescribed in this setting and the relationship to aftercare.
Method: Charts of 400 consecutive visits to the Psychiatric Emergency Service (PES) at an urban community hospital were systematically reviewed.

Results: (1) About half of PES visits resulted in admission to a psychiatric or detox unit. Among discharges, approximately 1/3 received a psychotropic prescription. (2) Of patients receiving prescriptions, antidepressants were most common (61%) followed by non-benzodiazepine sedatives (29%), benzodiazepines (22%), antipsychotics (16%), mood stabilizers (9%), and stimulants (3%). (3) Prescription of medication was significantly associated with;
a diagnosis of a depression, non-caucasian race, lower GAF score, and being married, employed, or domiciled. It was also associated with the absence of alcohol abuse, past hospitalizations, and current psychiatric treatment (p < 0.05). (4) Follow-up appointments were more likely to be given to those who did versus those who did not receive a prescription (p < .001). (5) However, those who received a prescription were not more likely to follow-through with referrals to outpatient treatment than those who did not receive a prescription.

Conclusions: A substantial number of patients who were discharged from this PES setting received a prescription, most often an antidepressant. Prescriptions were seldom given to those with greater historical illness burden (e.g., prior hospitalizations and substance abuse) and psychosocial disability (e.g., unemployment and homelessness). This raises concerns about their potential undertreatment and what barriers to care may exist. Accurate assessment and initiation of pharmacotherapy may not, however, ensure outpatient follow-up. These findings suggest a need to reevaluate the utility of and barriers to prescribing in the emergency setting.

References:

NR92 Monday, May 3, 9:00 a.m.-10:30 a.m.
Medical Characteristics of Emergently Medicated Psychiatry Patients
Tracy L. Schillerstrom, M.D., Department of Psychiatry, UTHSCSA, 7703 Floyd Curl Drive, San Antonio, TX 78229; Jason E. Schillerstrom, M.D., Sally Taylor, M.D.

Educational Objectives:
- At the conclusion of this session, the participant should be able to recognize that emergently medicated patients seen in a psychiatry emergency center are more likely to have abnormal medical laboratories compared to those not medicated.

Summary:
Objective: To determine the medical characteristics of patients receiving emergent intramuscular (IM) medications in a psychiatric emergency service (PES).
Method: A retrospective chart review of patients 18 years or older seen by a psychiatry emergency service over a 30 day period was performed. Demographic and laboratory variables were compared between patients receiving emergency IM medications and those not.

Results: Emergently medicated patients (n=35) were older than non-medicated patients (n=179) (42.6 years vs. 34.3 years, p<0.001). Patients receiving emergency IM medications had higher leukocyte count (p=0.04), blood urea nitrogen (p=0.001), creatinine (p=0.01), glucose (p=0.009), aspartate aminotransferase (AST) (p<0.001), alanine aminotransferase (ALT) (p=0.01), and electrocardiogram QTC interval (p=0.03). Patients receiving emergency IM medications were more likely to have abnormal levels of potassium (p<0.05), glucose (p<0.05), AST (p<0.001), and ALT (p<0.05). Abnormal glucose levels were more common in patients with laboratories collected after medication as opposed to before medication (p<0.05).

Conclusions: Patients receiving emergency IM medications in a PES are more likely to be older and have abnormal laboratory values. These results suggest this patient population may be more vulnerable to medications effecting liver function, kidney function, and glucose metabolism. These medical findings should be considered when emergently medicating patients in a PES.

References:

NR93 Monday, May 3, 9:00 a.m.-10:30 a.m.
Family Function and Psychosocial Well-Being Among Patients With Cancers
Chau-Shoun Lee, M.D., Department of Psychiatry, Poh-Ai Hospital, No. 83 Nan-Chang Street, Lo-Tung I-Ian 285, Taiwan; Jung-Chen Chang, Ph.D.

Educational Objectives:
- At the conclusion of this session, the participant should be able to understand the association between family functioning and individual psychosocial performance among patients with cancers.

Summary:
Objective: The study explored the relationship between family functioning and individual psychosocial wellbeing among patients with malignant diseases.
Methods: Newly admitted patients in an oncology unit were consecutively recruited. Patients and caregivers were interviewed by a psychiatrist to determine the psychiatric diagnoses and psychosocial wellbeing indicated by working, interpersonal interaction, and leisure-time activity. The APGAR scale was applied to assess family function on adaptation, partnership, growth, affection, and resolve.

Results: Of the 87 patients, 65 (74.7%) had ever had DSM-IV psychiatric disorders, commonly included delirium (N=28), adjustment disorder (N=22), and depressive disorders (N=19). The majority of them suffered from gastrointestinal (n=27), breast (n=16), and hematogenic (n=14) cancers. Their mean age was 45.2 ± 14.7, 48 (55%) male, 64 (74%) married, and educational years 8.5 ± 4.4. Cancer patients with higher family functioning in the APGAR scale were more likely to have good performance in their first-year lives with cancers even after controlling for demographics and the precancer functional level (β=−.23, p=.026, adjusted R²=.206).

Conclusions: Psychosocial wellbeing is important for quality of life in cancer patients. Clinical intervention to improve cancer patients' quality of life may strengthen the family functioning while considering patients' demographic, social, and cultural background.

References:

NR94 Monday, May 3, 9:00 a.m.-10:30 a.m.
Depression and Clinical Outcome in Renal Transplant Recipients
Gibi P. Rocha, M.D., Psychiatry Department, Pucrs Medical School, Rua marante 239 S404, Porto Alegre, RS 90430-181, Brazil; David Saitovitch, Ph.D., Mario B. Wagner, Ph.D., Paulo R. Zimmermann, M.D., Domingos Davila, Ph.D.
NR95          Monday, May 3, 9:00 a.m.-10:30 a.m.
Psychosocial Aspects of Xenotransplantation
David Teran-Escandon, M.D., Department of Psychiatry, Hospital Angeles, AV Universidad 1810 INT L1, Mexico City, OF 04310, Mexico; Luis A. Teran-Ortiz, M.S.C., Rafael Valdes

Educational Objectives:

At the end of this presentation, the participant should be familiar to the psychosocial factors involved in the xenotransplantation process.

Summary:

Introduction: Transplantation is a process with several psychosocial challenges, regarding xenotransplantation, the perceived similarity between humans and animals may be stressful. Adjustment disorders have been reported in transplantation recipients.

Objective: To assess the psychosocial aspects of xenotransplantation in porcine islet cell recipients and their efforts to adapt themselves to this condition.

Material and Methods: 10 insulin-dependent diabetes mellitus patients aged 14.58±1.93 who received porcine islet cells were included the patients and their parents were interviewed before the procedure about their expectations and overall functioning. The quality of life, enjoyment and satisfaction questionnaire and the hospital anxiety and depression scale were used. A 6-month follow-up was done. Statistical analysis was made using Wilcoxon’s test.

Results: Motivation was focused mainly in autonomy increase and simplify treatments, there were no troubles related to the cell source. There was a pragmatic view about xenografts, perceiving them as an unlimited resource. Affective status and QOL had nonsignificant improvements, except in sex life (p<0.05).

Discussion: Additionally to enthusiasm regarding xenotransplantation, using animals as an endless source of organs may affect patient’s compliance to treatment because this process can be repeated several times.

References:


Risk Factors for Mental Illness Among Asylum Seekers in Canada
Marc J. Miresco, M.D., Psychiatry Department, McGill University, 3463 Sainte-Famille #610, Montreal, PQ H2X 2K7, Canada; Laurence J. Kirkmayr, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to consider certain demographic variables as risk factors for mental illness among asylum-seekers.

Summary:
Objective: Asylum seekers have been found to have high rates of mental illness which may be related to pre-migratory trauma as well as to their reception in receiving countries, which is often based on policies aimed to deter refugee migration. This study explored potential risk factors for mental illness in this population.

Methods: A retrospective chart review of 2927 asylum seekers attending a regional medical clinic for refugees in Montreal, Canada in 1997 and 1998 documented sociodemographics and rates of mental illness, as indicated by any psychiatric diagnosis or symptoms, treatment or referral for psychological distress. Rates of acceptance of refugees into Canada according to country of origin were determined from 1998 United Nations statistics.

Results: There was wide variation in rates of mental illness by country of origin, ranging from 52.3% of Indian asylum seekers to 3.3% of Rwandans. There was also a marginally significant negative correlation of -0.58 (p=0.054) between rates of mental illness and rates of acceptance of refugee status according to country of origin.

Conclusions: Patterns of migration, exposure to trauma and cultural modes of coping may influence the experience and clinical recognition of psychological distress. A low likelihood of acceptance in the country of asylum may increase the psychological distress of asylum seekers during the period while they are awaiting determination of their claim for refugee status. Prospective research is needed to clarify this finding.

Funding: The study was supported by grants from Health Canada and the FRSQ.

References:

Early-Life Trauma and the Course of Bipolar I Disorder: A Pilot Study
Marc J. Miresco, M.D., Psychiatry Department, McGill University, 3463 Sainte-Famille #610, Montreal, PQ H2X 2K7, Canada

Educational Objectives:
At the conclusion of this session, the participant should be able to consider that early life trauma, such as physical or sexual abuse, may predispose a susceptible individual to a more severe form of Bipolar I disorder later in life.

Objective: To assess the independent relationship between early-life trauma, such as physical and sexual abuse, and major depression later in life, with overall CTQ score. The presence of suicidal ideations was associated with the overall CTQ score (p=0.044). The CTQ score also showed a trend of a correlation with the age of onset of the bipolar disorder (r=0.45, p=0.123).

Conclusions: Early-life trauma seems to be associated with certain measures of severity of Bipolar 1 Disorder later in life, though this study needs to be replicated using a larger sample.

References:

Immigration and Self-Perceived Emotional Health in Urban Primary-Care Patients
Supported by Eli Lilly and Company
Amalia Rosenblum, M.A., Epidemiology Department, Columbia University, 722 West 168th Street, New York, NY 10032; Raz Gross, M.D., Mark Olsson, M.D., Marc J. Gengoff, Ph.D., Amarendra Das, M.D., Adriana Feder, M.D., Myrna M. Weissman, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize that immigrants in an urban, primary care setting were more likely to report poor perceived emotional health even when major depression and other mental disorders were controlled for.

Summary:
Objective: To assess the independent relationship between immigration (defined as being born outside the USA) and poor perceived emotional health.

Methods: We used data from a mental health survey, conducted on a systematic sample (N=1,005) of urban primary care patients, to compare self-perceived emotional health of immigrants, mostly from the Caribbean, to that of non-immigrants. Information on self-perceived health was obtained using a 5-point Likert-scale, with poor and fair (vs. good, very good, or excellent) categorized as poor. Cross-linkage to the hospital’s computerized databases was used to obtain data on number of visits to the clinic.

Results: Immigrants were more likely to report poor perceived emotional health: 53.1% vs. 34%; odds ratio (OR)=2.19; 95% confidence interval (95%CI): 1.65-2.92; p<.0001. The results re-
mained significant after adjusting for ethnicity, socioeconomic sta-
tus, age, sex, major depression, and other common psychiatric
disorders, as well as self-perceived physical health (Adjusted OR=
1.63; 95%CI: 1.01-2.62; p=.045). Recency of immigration was not
related to poor emotional health. Immigrants did not make more
visits to the clinic (6.65±4.75 vs. 6.54±5.26 per year; p=0.76),
despite being more likely to report poor physical health (69.02% vs.
53.55%, p=0.001).

Conclusions: These findings suggest that immigrant patients in
primary care have unmet emotional health needs, not explained
by sociodemographic factors, physical health status, or psychiatric
conditions.

References:
and Mental Health: Mexican Americans in the United States.
Havard Review of Psychiatry: 8(2), 64-72.
2. Idler EL, and Benyamin Y, (1997) Self-Rated Health and Mor-
tality: A Review of twenty-seven community studies. Journal

NR100  Monday, May 3, 9:00 a.m.-10:30 a.m.
Inpatient Geropsychiatry Diagnoses in Hispanic
Elderly
Liliam Perez, M.D., Psychiatry Department, Zucker Hillside
Hospital, 75-59 263rd Street, Geriatric Psychiatry, Glen Oaks,
NY 11004; Elisse Ginsberg-Kramer, Ph.D., Neil Kremen, M.D.,
Michael Guberman, Blaine S. Greenwald, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able
to recognize phenomenologic and access issues in mental health
service delivery for minority aged.

Summary:
Background: Limited information is available on clinical charac-
teristics of Hispanic elderly who have accessed subspecialty geri-
atric psychiatry services. Several previous studies suggest differ-
ences in rates of clinical diagnostic diagnoses in African-American
older patients; whereas one large-scale Veteran’s Administration (VA)
study reported relatively few inpatient differences amongst
older Hispanics, Blacks, and Caucasians.
Methods: The intake ethnicity field was utilized to identify all
Hispanic patients over age 65 years (n = 83) admitted to the
Geriatric Psychiatry inpatient units at Zucker Hillside Hospital be-
tween - 01/2000 and 12/2003. These 83 medical record numbers
were matched by age to 83 randomly selected Black and Caucasian
patient medical record numbers admitted during the same
time period. The coded primary diagnosis was grouped into one
of seven categories. Diagnostic distributions were compared (chi-
square) to ascertain whether rates of dementia, psychosis, depres-
sion, bipolar illness, adjustment disorders, anxiety disorders,
and substance abuse/alcoholism differed across racial groups.
Results: Diagnostic categorization had been coded in 77%,
84%, and 81% of Caucasian, Black, and Hispanic patients. Overall
chi-square testing did not reveal significant differences in diagno-
sitic distributions across racial groups. Individual diagnostic com-
parisons demonstrated a trend-level difference (p = 0.07) in substance
abuse/alcoholism (3% Caucasian, 7% Black, 0% Hispanic).
Conclusions: Current findings in a voluntary, non-proprietary
psychiatric hospital’s distinct subspecialty geriatric psychiatry
units replicate prior VA findings of non-striking differences in diag-
nostic distributions amongst racial groups. That no older Hispanic
inpatient suffered from substance abuse/alcoholism suggests an
access barrier that merits further investigation.

References:
1. Kales HC, Blow FC, Bingham CR, Roberts JS, Copeland LA,
Mellow AM. Race, psychiatric diagnosis, and mental health
care utilization in older patients. J Geriatr Psychiatry 2000;
8:301-309.
2. Ruiz P. Hispanic access to health/mental health services. Psy-

NR101  Monday, May 3, 9:00 a.m.-10:30 a.m.
Psychiatrists’ and Psychologists’ Natural
Taxonomies of Mental Disorders
Elizabeth H. Flanagan, Ph.D., Psychology Department, Yale
University, Box 208205, 2 Hillhouse Avenue, New Haven, CT
06520-8205; Roger K. Blashfield, Ph.D.

Educational Objectives:
After viewing this new research, the participant should have a
better understanding of psychiatrists’ and psychologists’ concep-
tualizations of mental disorders as well as the relationship between
clinicians’ natural taxonomies and the DSM.

Summary:
Objective: Anthropologists and cognitive psychologists have
found that users of a classification system develop natural taxo-
nomies that are simpler and have fewer categories than the scient-
fic taxonomy (Berlin, 1992; Medin et al., 1997). The goal of this
research is to measure the natural taxonomies of mental disorders
that clinicians develop as a result of their clinical experience.
Method: In this study 17 psychiatrists and 18 psychologists
were given 67 DSM-IV diagnoses, and were asked to discard the
diagnoses with which they were not familiar. Then, they were
asked to sort the remaining diagnoses into groups that were “natur-
ally similar based on your clinical experience” and to put the
groups of diagnoses that were most similar next to each other.
Results: Results showed that psychiatrists were familiar with
more diagnoses that psychologists; both groups were less familiar
with the sleep, sexual, impulse control, and childhood disorders.
Principal component factor analysis showed consensus across
psychiatrists and psychologists in the organization of the diagno-
ses; however cluster analyses revealed some differences in psy-
chiatrists’ and psychologists’ sortings.
Conclusions: These data suggest that clinicians develop natural
taxonomies that are different from the scientific taxonomy, and
that there are some important differences in psychiatrists’ and
psychologists’ natural taxonomies.

References:
Princeton University Press.
tion and reasoning among tree experts: Do all roads lead to

NR102  Monday, May 3, 9:00 a.m.-10:30 a.m.
Psychiatric Morbidity and CHQ-12 in Patients With
Malignant Diseases
Jung-Chen Chang, Ph.D., Department of Health Management,
Ching-Kuo College, No. 83 Nan-Chang Street, Pohai Hospital,
Lo-Tung I-Lan 265, Taiwan; Chau-Shoun Lee, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able
to understand the psychiatric morbidity and the application of CHQ
in patients with malignant diseases.
Summary:
Objective: The psychiatric morbidity in cancer patients was neither well recognized nor appropriately managed. To understand the psychiatric morbidity and its recognition by self-administered questionnaire in cancer populations may advance clinical insights for consultation psychiatry.
Methods: The patients with cancers and admitted into an oncology unit was consecutively recruited. They were interviewed by a psychiatrist for the clinical psychiatric diagnoses and simultaneously filled a 12-item Chinese Health Questionnaire (CHQ-12) in which the score of 3/4 was used as the cut-off point.
Results: A total of 87 patients were recruited, mean age 45.2±14.7, 48 (55%) male, 64 (74%) married, and educational years 8.5±4.4. The mean (SD) and median scores of CHQ-12 were 3.3 (2.9) and 2.0, respectively. There were 49 (56.3%) were diagnosed as having a psychiatric disorder by interviewing, mainly adjustment disorders (n=22), depressive disorders (n=19), and other neurotic disorders (n=11). The sensitivity, specificity, and misclassification rate of the CHQ-12 were 57.1%, 84.2%, and 31.0%, respectively.
Conclusions: The clinical psychiatric interview had its irreplaceable value in the recognition of psychiatric morbidity among cancer patients. The implementation of self-administered questionnaire may be used as a source of additional information.
References:

NR104 Monday, May 3, 9:00 a.m.-10:30 a.m.
Outpatient Commitment in Manhattan: Diagnosis and Hospital Recidivism
Andrew M. Kleiman, M.D., Psychiatry Department, Bellevue Hospital, 462 First Avenue, 21W24, New York, NY 10016; Gary R. Collins, M.D., Michael J. Magera, M.D., Devin Stroman
Educational Objectives:
At the conclusion of this session, the participant should be able to demonstrate a basic understanding of the Manhattan Assisted Outpatient Treatment Program and recognize its possible benefits to the severely mentally ill person diagnosed with Schizophrenia, Schizoaffective Disorder, Bipolar Type, and Bipolar Disorder, in terms of a decreased number of hospitalizations and a decreased total number of inpatient hospital days.
Summary:
Objective: To evaluate the effectiveness of Manhattan's Assisted Outpatient Treatment (AOT) program in reducing number of hospital admissions, and total number of inpatient hospital days, from New York City's mentally ill population with a focus on the impact of psychiatric diagnosis.
Method: The authors examined the first 46 clients alphabetically who have been treated in Manhattan under AOT. Of these, forty clients' charts contained complete data for the year prior to the initial AOT order and the year following the order. Twenty one clients were diagnosed with Schizophrenia, ten with Schizoaffective Disorder, Bipolar Type, and nine with Bipolar Disorder.
Results: AOT clients, regardless of DSM-IV diagnosis, were significantly less likely to be hospitalized and were hospitalized for significantly fewer days in the year following AOT enrollment compared to the year prior to AOT enrollment. Examining specific diagnoses, AOT was effective in patients with Schizophrenia (0.42 admissions v. 1.67 admissions) (40.0 days v. 184.1 days), Schizoaffective Disorder (1.0 admissions v. 2.1 admissions) (27.2 days v. 172.3 days), and Bipolar Disorder (0.67 admissions v. 2.3 admissions) (15.0 days v. 107.7 days).
Conclusions: This initial study suggests that the court ordered AOT Program was clinically beneficial to its clients, across a range of DSM-IV diagnoses. Future study includes differentiating the effectiveness of AOT within diagnostic categories.
References:
NR105  Monday, May 3, 9:00 a.m.-10:30 a.m.
Substance Disorders and Manhattan’s Assisted-Outpatient Treatment Program
Michael J. Magara, M.D., Psychiatry Department, Bellevue Hospital, 462 First Avenue, 21W18, New York, NY 10016; Gary R. Collins, M.D., Andrew M. Kleiman, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to demonstrate an understanding of treatment issues and outcomes in chronically mentally ill patients with and without co-morbid substance-related disorders subject to an outpatient commitment order, where primary outcome measures include a reduction in number of hospitalizations and a decrease in the total number of inpatient hospital days.

Summary:
Objective: To evaluate the effectiveness of an outpatient commitment order, with concurrent intensive services, in reducing hospital readmissions and the total number of inpatient hospital days for chronically mentally ill patients with and without co-morbid substance disorders.
Method: The authors randomly examined charts of 48 clients treated in Manhattan under AOT. Complete data was available for forty clients during the year prior to AOT and during the first year of AOT enrollment. Twenty-two clients were dually diagnosed and eighteen had a major Axis I disorder without a co-morbid substance condition.
Results: A substantial reduction in the number and duration of hospitalizations was found in both groups, though a more pronounced decrease occurred in the population without a co-morbid substance disorder. Dually diagnosed clients had a mean of 1.86 admissions/person (239.32 hospital days/patient) one year prior to AOT vs. 0.91 admissions (48.95 days) during their first year enrolled in AOT. Non-substance using patients had 2.11 admissions (117.11 days) one year pre-AOT and 0.67 admissions (29.89 days) in the year following AOT enrollment.
Conclusions: This data suggests clinical benefit from outpatient commitment in both groups of patients. However, further investigation is required to assess the differential effectiveness of court-mandated treatment, especially among clients with significant substance-related illness.

References:

NR106  Monday, May 3, 9:00 a.m.-10:30 a.m.
The Study of the Subjective Symptoms of Traumatic Brain Injury Patients Using Structured Evaluation Scale and Neuropsychological Tests
Jongbum Lee, M.D., Psychiatry Department, Yeunam University Hospital, Daemyung Dong Nambu, Daegu 705-717, South Korea; Seungdeuk Cheung, M.D., Jinsung Kim, M.D., Wanseok Seo, M.D., Shinho Song, M.D., Eunjung Jung, M.D.

Educational Objectives:
At the conclusion of this session, psychotic symptoms was mainly used for the taking bad of symptom and proved that they underestimated their psychiatric symptoms with better cognitive function level after traumatic brain injury.

Summary:
To search for the character of subjective symptom among traumatic brain injury(TBI) patient we tried to investigate the level of subjective symptoms and the character of the discrepancy between subjective symptoms and suggested disability SCL-90-R, K-WAIS, K-MAS, K-BNT and MMPI was conducted for two hundred eighty one patients who are suitable for this study with age over 18. In the result of SCL-90-R depending on the subjective symptom level, there was significant difference in subscale and global index of SCL-90-R. The result of neuropsychological test depending on the level of subjective symptoms represented more severe in subjective symptoms and lower in intelligence after TBI. But, even or better intellectual capability was possessed in faking good group by comparing to no difference group. Memory ability is reduced as subjective symptoms severe and faking good group was superior in its performance as a result of memory test depending on subjective symptoms. The same result was shown in K-BNT. Regardless of the level of subjective symptoms or discrepancy of the subjective symptoms between suggested disability, TBI patients experienced basic neurotic symptoms and they appealed psychotic symptoms as the level of subjective symptoms is severe in MMPI. In this research, all the patient commonly have experienced neurotic symptom weather the symptom of traumatic brain injury patients is severe or not. Psychotic symptoms was mainly used for the faking bad of symptom and proved that they underestimated their psychiatric symptoms with better cognitive function level after TBI.

References:

NR107  Monday, May 3, 9:00 a.m.-10:30 a.m.
The Effects of Intellectual Level on Behavioral Symptoms and Executive Functions in Children With ADHD
Jongbum Lee, M.D., Psychiatry Department, Yeunam University Hospital, Daemyung Dong Nambu, Daegu 705-717, South Korea; Seungdeuk Cheung, M.D., Jinsung Kim, M.D., Wanseok Seo, M.D., Shinho Song, M.D., Eunjung Jung, M.D.

Educational Objectives:
At the conclusion of this session, intellectual level of children with ADHD is influenced by higher executive functions supervising attention and information processing rather than by attentional capacity.

Summary:
This study was performed to investigate psychopathology, behavioral symptoms, attentional and executive functions of ADHD children according to intellectual function level. We studied one hundred ninety-seven children outpatient, diagnosed ADHD by the DSM-IV who visited department of neuropsychiatry of Yeungnam University Medical Center, we divided ADHD children based on intellectual function level by K-ABC and compared their K-PIC, Korean version of ADDES-HV, ACTeRS, CAP, SNAP, Connets, CPT, WCST results. There were significant differences in results of K-PIC, at scale of verbal development (p<.01), socialization (p<.05) and autism (p<.01). Inattention subscale of CAP (p<.05) and SNAP (p<.05) results showed significant differences according to intellectual function level. In CPT results, there were no significant differences. In WCST results, ADHD with lower level of intellectual function showed significantly lower level of
performance in total number of errors (p<.01), perseveration errors (p<.05), number of categories complete (p<.01), and trials to complete first category (p<.05). Intellectual function level of ADHD had relation to disabilities in K-ABC and behavioral check list. But attention and impulsivity of CPT had no correlation with intellectual function level of K-ABC. Executive function such as abstract thinking categorization, working memory, flexibility of WCST had significant relation to intellectual function level in ADHD children. Therefore intellectual level of children with ADHD is influenced by higher executive functions supervising attention and information processing rather than by attentional capacity.

References:

NR108  Monday, May 3, 9:00 a.m.-10:30 a.m.
Quantitative Trait Analysis of the GABA Beta Receptor 1 Gene in OCD
Gwyneth C.M. Zai, Neurogenetics, Centre for Addiction and Mental Health, 250 College Street, Toronto, ON M5T 1R6, Canada; Nicole A. King, Eliza Burroughs, B.A., Cathy L. Barr, Ph.D., James L. Kennedy, M.D., Margaret A. Richter, M.D.

Educational Objectives:
- At the conclusion of this session, the participant should be able to understand the genetic basis of OCD; to understand the involvement of the GABAnergic system in the development of OCD.

Summary:
Introduction: Obsessive-compulsive disorder (OCD) is a severe neuropsychiatric illness. Genetic factors are believed to be etiologically important. Although researchers have focused on the serotonergic and dopaminergic systems, increasing evidence suggests that the major inhibitory neurotransmitter, gamma-amino butyric acid (GABA), may also be involved. Furthermore, the GABA beta receptor 1 (GABABR1) gene has been localized to chromosome 6p21.3 region, which has shown linkage to OCD. Methods: We investigated the transmission of alleles and haplotypes from five polymorphisms (-7265A/G, 10497C/G, 3'-UTR to 33795A/G substitutions; Ser491Ser-1473T-» C, Phe659Phe-1977T-» C) in the GABABR1 gene in 175 DSM-IV OCD probands and their families, using the transmission disequilibrium test and TRANSMIT. Results: We did not observe association between OCD and any polymorphism individually. However, a trend toward association with the 1.2.2.1.1 haplotype (Ser491Ser.A-7265G.Phe659Phe.A33795G.C10497G) with a p-value of 0.06 (overall x²=6.35, 5 d.f., P=0.27) and toward the YBOCS severity score in the Phe659-Phe polymorphism (z=1.827, P=0.07) were detected. Conclusion: The observed trends suggest that further investigations of the role of the GABABR1 gene in OCD are warranted.

References:

NR110  Monday, May 3, 9:00 a.m.-10:30 a.m.
Task Variability Related to Functional Status in Old Age
Michael A. Rapp, M.D., Psychiatry Department, Mt. Sinai Medical School, 1 Gustave Levy Place, New York, NY 10029, Jeremy Silverman, Ph.D., Mary Sano, Ph.D., Vahram Haroutunian, Ph.D.

Educational Objectives:
- At the conclusion of this session, the participant should be able to understand the role of task variability in aging and its relationship to functional status.
that postural control is preserved by adaptive resource allocation towards tasks of higher immediate value (e.g., postural control) of successful aging as selective optimisation with compensation control and working memory. With increasing difficulty in the pos-
tasks decreases, a pattern exaggerated in Alzheimer’s disease.

To understand the role of multitasking for functional status in aging even in AD.

At the same time, recent research indicates a preference of older 
adults to allocate their restricted resources within multiple tasks 
As an example of adaptive resource allocation. Here we show 
Summary:

Educational Objectives:

References:

NR112 Monday, May 3, 9:00 a.m.-10:30 a.m. Antipsychotic Use in the Elderly: Shifting Trends and Increasing Costs

Mark J. Rapoport, M.D., Department of Psychiatry, University of Toronto, FG22-2075 Bayview Avenue, Toronto, ON M4N 3M5, Canada; Muhammad Mamdani, M.A., Kenneth I. Shulman, M.D., Nathan Hermann, M.D., Paula Rochon, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to understand and appreciate the increasing costs associated with changing trends in antipsychotic utilization in the elderly over the last ten years.

NR111 Monday, May 3, 9:00 a.m.-10:30 a.m. Selective Resource Allocation to Postural Control in Alzheimer’s Disease

Michael A. Rapp, M.D., Psychiatry Department, Mt. Sinai Medical School, 1 Gustave Levy Place, New York, NY 10029; Ralf T.H. Krampe, Ph.D., Paul B. Baltes, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to understand the role of multitasking for functional status in aging and Alzheimer’s disease.

Summary:

Objective: To assess trends in utilization and costs of antipsychotic drugs among an elderly population over time with respect to the prevalence of users, shifts in prescribing patterns, and related financial implications.

Method: A population-based study of more than 1.4 million residents of the province of Ontario aged 65 years or older was conducted. Cross-sectional time series of quarterly and annual antipsychotic utilization and cost were obtained from administrative databases for calendar years 1993 through 2002.

Results: The prevalence of antipsychotic users increased by 34.8% over the study period from 2.2% at the beginning of 1993 to 3.0% of the elderly at the end of 2002. This was associated with a 229.5% increase over the duration of the study period in total annual number of prescriptions dispensed, and a 948.6% increase in total costs (from $3.7 million to $31.4 million in 2002). The atypical antipsychotics, which were not available in 1993, made up 82.4% of the antipsychotics dispensed and 95.2% of costs in 2002.

Conclusions: The modest increase in antipsychotic prevalence in the elderly over the last ten years has been associated with a substantial increase in utilization and cost, with a significant shift towards use of the atypical antipsychotics.

References:


NR113 Monday, May 3, 9:00 a.m.-10:30 a.m. Brain Injury In Older Adults: A Longitudinal Study

Mark J. Rapoport, M.D., Department of Psychiatry, University of Toronto, FG22-2075 Bayview Avenue, Toronto, ON M4N 3M5, Canada; Andrea Phillips, B.A., Anthony Feinstein, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to understand about persisting psychiatric and psychosocial
sequelae of mild-to-moderate traumatic brain injury in older adults one year after injury.

Summary:
Objective: To explore for the persistence of psychiatric and physical morbidity one year after traumatic brain injury (TBI) in older adults.

Methods: Forty-one participants aged 50 to 89 discharged from a trauma center with acute mild-to-moderate TBI were compared to fifty-four matched controls for assessments at three, six, and twelve months post-injury. Major depression was assessed using the structured interview for DSM-IV; psychological distress, psychosocial functioning, and physical symptoms were assessed using serial self-report instruments.

Results: Major depression was seen in 19% of cases at 3 months post-injury, and 16% at one year post-injury, compared to no controls at 3 months and 2% of controls at one year ($t_{(76)}=2.00, p<0.05$). Although cases had low scores on self-reported measures, they had significantly higher levels of psychological distress ($t_{(165)}=2.39, p<0.02$), psychosocial dysfunction ($t_{(165)}=2.60, p<0.01$), and physical symptoms ($t_{(164)}=5.61, p<0.0001$) than controls at all time points.

Conclusions: Similar to studies in younger TBI patient samples, the current study demonstrates that although there is generally good outcome one year after mild-to-moderate TBI in older adults, physical and psychosocial problems are greater than similar controls, and major depression has a high prevalence.

References:

NR115 Monday, May 3, 9:00 a.m.-10:30 a.m.
Falls Assessment in a Chronic-Care Facility
Hima B. Palakurthi, M.D., Department of Psychiatry, Hershey Medical Center, 500 University Drive, Hershey, PA 17033; Paul A. Ketti, M.D.

Educational Objectives:
At the completion of this session, the participant should be able to identify various modifiable risk factors for falls in a Chronic Care Facility.

Summary:
Falls are a common and potentially serious problem among elders hospitalized in a chronic care setting. However, little data is available on risk factors for falls.

Method: All falls in a 28 bed geriatric unit in a Chronic Care Facility were reviewed retrospectively over a period of 8 months. Twelve patients had more than 2 falls during this time. They were compared to 10 patients who did not fall on a variety of risk factors, like psychiatric diagnoses, treatment and functional abilities of those patients. The groups were compared using chi square statistics, with $p=0.05$ chosen as a significance level.

Results: The fall rate on the ward was 0.0133 falls/patient/day. Patients who fell differed by having higher incidence of the following factors: treatment with medications like olanzapine and depakote, axis II diagnosis, low baseline physical functioning. Of the above factors, olanzapine usage significantly increased the number of falls, compared to the negligible increase by others.

Conclusion: Based on this small series, olanzapine use may be associated with a higher risk of falls. Further research is indicated in this important health outcome for elders receiving chronic psychiatric care.

References:
C.S.W., Elisse Ginsberg-Kramer, Ph.D., Blaine S. Greenwald, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to better understand the consequences and determinants of burden and morale in dementia caregivers.

Summary:
Background: A large literature demonstrates an inverse relationship between ADL/IADL in memory impaired patients and level of burden in their caregivers. However, surprisingly limited information is available on the relationship of ADL/IADL and caregiver morale. Although overlap exists on scale items, burden typically reflects day-to-day inconveniences and excess tasks associated with caregiving; whereas diminished morale is likely a more multi-determined phenomena reflecting a psychological melange of unhappiness, dysphoria, dissatisfaction, and pessimism. The purpose of the present study was to dissect out the impact of patient ADL/IADL performance on caregiver morale.

Methods: Seventy-two (72) patients with memory complaints and their caregivers were screened in a special Memory Disorders Program. In addition to cognitive, neurobehavioral and multidimensional geriatric assessments, patients ADL and IADL performance were rated using the Duke University Older Americans Resource Scale (OARS) methodology. Caregivers were contemporaneously assessed on measures of burden (Zarit Index) and morale (PGC Morale Scale). The relationship between patient ADL/IADL and caregiver measures was examined using multiple regression analysis.

Results: IADL, but not ADL, was found to be a significant predictor of caregiver burden (p = 0.02). In contrast, neither ADL or IADL predicted caregiver morale.

Conclusions: Significant IADL-burden findings are consistent with a large prior literature. The somewhat unexpected lack of relationship between ADL/IADL and morale supports that (a) morale and burden are distinct entities; and (b) other potentially modifiable determinants of caregiver morale should be sought.

References:

Educational Objectives:
At the conclusion of this session, the participant should understand the common impairments in executive function across different impulsive, addictive groups.

Summary:
Objectives: The development of evidence-based clinical practice guidelines (EBPG) should incorporate information on patient factors such as age, gender, and ethnicity, particularly in dementia which is more prevalent among minorities. EBPG in the treatment of dementia recommends the use of antipsychotic medications to treat psychosis of dementia. The study aims to examine the evidence base referenced in EBPG for demographic information to determine the generalizability of the results.

Methods: Computerized medical literature databases were reviewed to obtain demographic information on the studies that describe the efficacy and safety of antipsychotics to treat behavioral disturbances or psychosis in older adults with dementia. Results: 134 studies were identified in the medical literature. Of these, 20 were referenced in treatment guidelines bibliographies. 3142 subjects participated in these studies. 16 studies reported no data. The 4 studies reporting demographics were: 1340 (92%) White non-Latino; 23 (1.6%) African-American; 5 (0.3%) Latinos; 4 (0.3%) Asian-Americans; 86 (5.7%) Other.

Conclusions: The EBPG for the treatment and management of psychosis in dementia fail to address race/ethnicity. Clinicians must take this into account, recognizing that efficacy and safety parameters may be different for their ethnic minority patients. Future research in this area should actively recruit ethnic minority participants.

References:
controls on measures of executive function, although pedophiles showed greater impairment than the other groups. Further research could determine whether such impairment generalizes to larger samples, and whether it reflects specific cognitive deficits such as visual-spatial impairment, or a more general impulsive cognitive style.

References:

NR119  Monday, May 3, 9:00 a.m.-10:30 a.m.
Pathological Gambling Secondary to Dopamine Agonist Therapy in Parkinson’s Disease
Dominique Drapier, M.D., Hopital G. Regnier, 108 Avenue Gal Leclerc, Rennes 35000, France; Sophie Drapier, M.D., Pascal Derkinderen, M.D., Francois Lallemand, M.D., Philippe Damier, M.D., Marc Verin, M.D., Bruno Millet, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize and diagnose a pathological behavior associated with dopamine agonist in Parkinson’s disease.

Summary:
We describe 6 patients with Parkinson’s disease and pathological gambling. This association has been poorly reported. Patients met Diagnostic and Statistical Manual and Mental disorders, 4th edition, criteria for pathological gambling. All patients underwent a neurologic and psychiatric examination, specifically noting the presence or absence of psychopathology in the spectrum of impulse control disorder and the nature of the gambling. The mean age of the subjects was 51.6 years and the mean duration of PD from time of diagnosis was 5.6 years. A previous history of depression was reported for two patients. All patients started gambling after the onset of Parkinson’s disease and treatment with dopaminergic agonist. Slot machines and internet sites were the preferred source of gambling. That the pathological behavior begins with the introduction or the increase of the dopaminergic agonist and that the behavior disappeared at the medication end, suggest that it could be related to the dopaminergic tone in patients with Parkinson’s disease (that is, it could represent an elaborated behavioral manifestation of a pharmacological treatment).

References:

NR120  Monday, May 3, 9:00 a.m.-10:30 a.m.
A Pilot Intervention to Change Physician Behavior
Cathryn A. Galanter, M.D., Psychiatry Department, Columbia University, NYSPH, 1051 Riverside Drive, 78, New York, NY 10032; Lawrence V. Amsel, M.D., Elizabeth Pappadopulos, Ph.D., Peter Gollwitzer, Ph.D., Gabriele Oettingen, Ph.D., Peter S. Jensen, M.D.

Educational Objectives:
At the conclusion of this presentation, participants will have increased knowledge on an effective basic behavioral science method that assists physicians in implementing practice guidelines.

Summary:
Objective: This pilot assesses an intervention to change physician practice behavior.
Background: Traditional continuing medical education (CME), such as lectures and the distribution of practice guidelines, has limited impact on clinical practice. Therefore, after Columbia University and New York State developed consensus practice guidelines, Treatment Recommendations for the Use of Antipsychotics for Aggressive Youth (TRAAY), we also adapted a basic behavioral cognitive science intervention, Mental Contrasting-Implementation Intentions (MCII) to work with physicians to change their behavior. MCII has effectively assisted people in changing their behavior, but has never been applied to physicians.

Method: Over 4 months, 5 physicians treating inpatient children and adolescents received one CME lecture and 6 individual MCII sessions. Physicians completed pre- and post-intervention questionnaires on behavioral intentions, attitudes towards TRAAY, and a modified Working Alliance Inventory.

Results: Five physicians completed the interventions. Behavioral intentions to use TRAAY improved for 3 of 4 targeted guidelines. Three of 4 guidelines were perceived more favorably and easier to implement. Perceptions of the strength of 8 of 12 obstacles decreased. Participants rated the consultation positively overall.

Conclusions: Results show improved attitudes and intentions to use guidelines but should be interpreted cautiously in view of no random assignment or control group.

References:

NR121  Monday, May 3, 9:00 a.m.-10:30 a.m.
Improving Funding and Recruitment by Teaching College Undergraduates
Kenneth J. Braslow, M.D., Psychiatry Department, University of Texas, San Antonio, 128 Katherine Court #2, San Antonio, TX 78209; Daniel J. Feeney, M.D., Kenneth L. Matthews, M.D., Anneke C. Bush, Sc.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize that teaching college undergraduates about psychiatry may help recruitment in the field at large and provide significant funding to departments that provide this type of course.
NR122  Monday, May 3, 9:00 a.m.-10:30 a.m.
Comparing Shelter-Using and Non-Shelter-Using Homeless Individuals in Phoenix
Ernest Poortinga, M.D., University of Michigan, 1500 East Medical Center Drive, Ann Arbor, MI 48106; Larissa Larsen, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize psychosocial demographic and clinical predictors of service utilization in a homeless population.

Summary:
Research has revealed that homeless individuals are not a homogenous group of individuals but are members of distinct subpopulations united by a common need for shelter. Very little research has been done to understand the subpopulation of homeless individuals who avoid services. Using a case control study design, this study compared the characteristics of 85 homeless individuals who used shelter services (including a mental health clinic) with 45 homeless individuals who chose not to use shelters in Phoenix, Arizona. Survey results were first analyzed at the univariate level. Independent variables showing between group differences at \( p \leq 0.25 \) were then entered into a logistic regression model. The homeless individual who opted not to use services was more likely to have experienced court ordered psychiatric treatment (Adj. O.R. = 7.70 with 95% C.I. = 1.62-36.6), consumed larger quantities of alcohol more regularly (Adj. O.R. = 3.47 with 95% C.I. = 1.30-9.29), was more likely to be Native American (Adj. O.R. = 4.62 with 95% C.I. 0.84-25.41), and more frequently worked as a day laborer (Adj. O.R. = 2.79 with 95% C.I.O. .88-8.89). These findings may assist community mental health providers design outreach programs for homeless persons with mental illness. A Motorola/Arizona State University ‘Great Communities Seed Grant’ funded the project.

References:
Educational Objectives:
At the conclusion of this session, the participant should be able to recognize long term effects from the terrorist attacks.

Summary:
Objective: We previously reported that approximately ten percent of Japanese living in New York presented with probable Post Traumatic Stress Syndrome (PTSD) three months after the World Trade Center terrorist attacks. We conducted a follow-up study to determine long term effects from the terrorist attacks.

Method: A set of questionnaires was distributed to 502 Japanese families living in NY in September 2002 one year after the attacks. It included demographic and disaster-exposure questions and impact of Event Scale—Revised (IES-R).

Results: 180 families responded. 141 of the responders lived in NY before the attacks and 39 of the responders moved to NY after the attacks. In 141 responders living in NY before the attack 10.2% of the children, 7.1% of their fathers and 2.5% of the mothers presented with probable PTSD. The children and their fathers exposed to the attacks had statistically significant high IES-R than ones not exposed to the attacks (p= 0.009, p=0.016 respectively). Among Japanese who lived in NY on September 11, 2001, psychological trauma measured by IES-R was associated with emotional physical, TV exposure to the attacks.

Conclusions: This survey revealed that Japanese exposed to the terrorist attacks continued to exhibited high levels of PTSD like symptoms.

References:

NR125 Monday, May 3, 9:00 a.m.-10:30 a.m.
Identifying Factors That Contribute to Physician Work Stress
Henry A. Bollini, M.D., Psychiatry Department, Ehring Burquist, 55 MDOIS/SGOH, 2501 Capehart Road, Offutt AFB, NE 68113-2160; Joseph P. Chozinski, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to identify organizational and personal factors that contribute to physician work stress and performance problems.

Summary:
Objective: Physicians have an increased prevalence of psychological stress. The aim of this study was to examine factors that may significantly affect the perceived occupational stress in a population of medical residents.

Method: The sample consisted of 132 physicians involved in postgraduate training who voluntarily completed a 42-item questionnaire and NEO-s Personality Inventory.

Results: Spearman’s correlations were calculated between the various outcome measures to determine significance (α < 0.05). The strongest correlate to perceived work stress was the NEO-s Neuroticism scale (0.535). In a subset with low Neuroticism scores, the factors that remained significantly correlated to work stress were the availability of leisure/vacation time (0.283), the NEO-s Neuroticism scale (0.271), use of leisure time (−0.265), senior colleague support (−0.251), general health status (0.229) and identity strength (0.202). Work performance problems were also significantly correlated with the availability of leisure/vacation time (−0.278) and positive feedback (−0.163).

Conclusion: The organizational factors most important for reducing occupational stress in physicians and improving work performance are: availability of leisure/vacation time, senior colleague support, and positive feedback. The personal factors most important to occupational stress include: NEO-s defined Neuroticism, use of leisure time, general health status, family stress, and identity strength.

References:

NR126 Monday, May 3, 9:00 a.m.-10:30 a.m.
Restraint Stress-Induced, Depression-Like Behavior Is Abolished by Electroconvulsive Stimulation
Martin B. Jorgensen, M.S.C., Laboratory of Neuropsychiatry, Rigshospitalet, Blegdamsvej 9, Copenhagen, DK 2100, Denmark; Ida Hageman, M.D., Gitta Wortwein, Ph.D., Tom G. Bolwig, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize that restraint stress in rats causes behavioural changes and that this effect can be modulated by treatment (ECS).

Summary:
Objective: The objective of this study was to investigate the modulating effect of electroconvulsive stimulations (ECS) on behavioural effects of restraint stress.

Methods: 48 male Sprague-Dawley rats (250-300 g), were allocated to four groups: 1) 12 rats were subjected to 6 hours of restraint stress daily for 21 days, 2) 12 rats underwent the same stress paradigm plus ECS three times a week, 3) 12 rats received 3 weekly ECS and 4) 12 rats were left undisturbed in their cages except for daily handling. After the last stress session the rats were tested for immobility and explorative behaviour in the Forced Swim Test².

Results: Stressed rats had significantly higher increases in immobility in the Forced Swim Test than non-stressed rat. Rats treated with ECS had significantly lower increases in immobility than stressed rats and control rats. Furthermore stressed rats displayed less explorative behaviour compared with control rats and especially in comparison with ECS treated rats.

Conclusions: Restraint stress elicits increased immobility in the Forced Swim Test. Furthermore stressed rats displayed less explorative behaviour than control and ECS treated rats. These behaviours are seen as animal “despair” and can be regarded as depression-like behaviour.

References:
NR127  Monday, May 3, 9:00 a.m.-10:30 a.m.
Assaultive Behavior, Impulsivity, and Completed Suicide in Adolescents
Sebastien Collette, M.D., Psychiatry Department, Ste. Lusitne Hospital, 3175 Cote Ste. Catherine, Montreal, QC H3S 1W3, Canada; Johanne Renaud, M.D., Alain D. Lesage, M.D., Michel Toussignant, Ph.D., Francois Chagnon, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize assaultive, and negative behaviors as well as impulsivity, as risk factors for completed suicide in adolescents.

Summary:
Objective: Few studies have examined adolescent suicide in Canada. This study reports on assaultive and impulsivity in adolescent suicide victims compared to a community sample from the Province of Quebec.

Methods: Reports from the coroner’s office were screened, and parents of suicide victims aged less than 19 years old (n = 33) were recruited through mail. Parents of the community sample (n = 10) were recruited through schools and local community service centres. Both groups were interviewed using the psychological autopsy method. The Barratt Impulsiveness Scale (BIS-11), the Buss and Durkee Hostility Inventory (BDHI) and the Brown Goodwin Lifetime History of Aggression (BGHLA), three self report forms, were filled by the parents concerning the decreased or the living youth control.

Results: Using the BDHI, the suicide victims showed more assaultive (p < 0.001) and negative behaviors (p=0.034) compared to the community sample. They were also found to be more impulsive (p = 0.029) on the BIS-11 scale. There were no significant differences between the two groups with respect to other subscales of the BDHI and the BGHLA.

Conclusion: Our preliminary results suggest that assaultive and negative behaviors, and impulsiveness, should be considered as risk factors for completed suicide in adolescents.

References:

NR128  Monday, May 3, 9:00 a.m.-10:30 a.m.
Youth Suicide Risk Factors and Attitudes in New York and Vienna
Kanita Dervic, M.D., Child Psychiatry Department, University of Vienna, Wahringer Gurtel 18-20, Vienna 1090, Austria; Madelyn Gould, Ph.D., Gerhard Lenz, M.D., Marjorie Kleinman, M.S., Drew M. Velting, Ph.D., Tuerkan Akkaya-Kalayci, M.D., Max H. Friedrich, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to:
1. To gain knowledge of the nature and extent of adolescents attitudes towards suicide and suicide risk factors in New York and Vienna; 2. To assess possible cross-cultural differences.

Summary:
Background: Adolescents attitudes towards suicide and prevalence of suicide risk factors in New York and Vienna were compared in order to explore possible cross-cultural differences.

Methods: New York (n=2419) and Viennese (n=214) high school students were surveyed using a self-report questionnaire developed for a suicide screening project in New York.

Results: A higher depression rate (14.5% vs. 9.8%, p<0.05) and more first-hand experience with a suicidal peer (45.2% vs. 33.6%, p<0.001) were found in Vienna. More attribution of suicide to mental illness was found in Viennese adolescents (24.8% vs. 16.8%, p<0.01). Students in Vienna were more likely than those in New York to keep secret a friend’s suicidal intentions (82.7% vs. 7.7%, p<0.001). The Viennese youth was also more likely to think that people who speak about suicide do not commit it (44.9% vs. 27.5%, p<0.001), and were more often endorsing suicide as a possible solution to problems (19.6% vs. 12.8%, p<0.05). With regard to help-seeking behavior, the Viennese youth was significantly less likely to recommend a suicidal friend to use hotline service than their counterparts in New York (26.2% vs. 44.2%, p<0.001).

Conclusions: After controlling for demographic differences, level of depression and previous first-hand experience with a suicidal peer, the results suggest that a socio-cultural context may underlie the differences between American and Austrian adolescents in their attitudes towards suicide.

References:
The results of this study offer a glimpse into social information processing deficits as potential precursors of impulsive aggression.

References:

NR130  Monday, May 3, 9:00 a.m.-10:30 a.m.
The Relationship Between Aggression, Executive Functioning, and Intermittent Explosive Disorder Supported by National Institutes of Health

Michael S. McCloskey, Ph.D., Department of Psychiatry, University of Chicago, 5841 South Maryland Avenue MC3077, Chicago, IL 60637, Royce J. Lee, Kurtis L. Noblett, Ph.D., Emil F. Coccaro, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize that Intermittent Explosive Disorder is associated with increased aggression and decreased executive functioning.

Summary:
Objective: To determine the relationship between Intermittent Explosive Disorder (IED), aggressive behavior and executive functioning.
Method: Twenty-eight participants with IED and 57 non-IED control participants completed a laboratory measure of executive functioning (Bechara Gambling Task) as well as a measure of laboratory aggression in which the participant administers varying levels of shock to a fictitious opponent (Taylor Aggression Paradigm). IED Diagnoses were determined via a structured clinical interview (Intermittent Explosive Disorder Module).
Results: Participants with IED set higher levels of shock for their opponent in comparison to participants without IED both prior to provocation and in response to provocation (both p < .05). Furthermore, when compared to the non-IED group, participants with IED also demonstrated diminished learning in the executive functioning task (p < .05). Learning on the executive functioning task was associated with the level of shock administered by the non-IED group but was unrelated to shock selection in the IED group.
Conclusions: Individuals with IED are more prone to aggressive responding than non IED individuals independent of provocation. Individuals with IED also have deficits in executive functioning, a process that appears to be related to aggressive responding in non-IED individuals.

References:

NR132  Monday, May 3, 9:00 a.m.-10:30 a.m.
Prior Psychiatric Diagnosis and Life Events in Fibromyalgia Patients

Marta Alda Diez, M.D., Department of Psychiatry, Miguel Servet Hospital, Isabel la Catolica 1, Zaragoza 50008, Spain; Javier Garcia-Campayo, M.D., Elida Pascual, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize and discuss about predictors in male genital self-mutilation.

Summary:
Objective: This study was undertaken to identify the psychiatric aspects in patients with genital self-mutilation in Korea.
Method: The authors investigated sixteen cases in terms of general epidemiological characteristics, the nature of mutilation, diagnostic classification, mental status and psychopathology at the time of the act, psychodynamics of their behavior and risk factors.
Results: In terms of the mutilation types and instruments, transaction of penis type were committed most frequently(93.8%), mostly by knives(68.8%). Almost all of them felt comfortable after the act of self-mutilation(93.8%). The formal diagnoses of the subjects were mainly schizophrenia(87.5%). Major symptoms at the time of the act were delusion and/or hallucination(41.7%) and depressive state(29.2%). Psychodynamically, lots of cases could be explained as to punish failures in the male role(21.9%), related to religiosity (15.6%), and the wish to be or delusion of being female(12.5%).
Conclusions: The findings suggest that the risk factors for the genital self-mutilation are the deprivation of the early experiences, presence of psychotic disorder or depression, identity confusion, and the guilty feelings toward sexual aggression.

References:

NR131  Monday, May 3, 9:00 a.m.-10:30 a.m.
Psychiatric Aspects of Male Genital Self-Mutilation in Korea Supported by GlaxoSmithKline

Sang Hoon Kim, M.D., Department of Psychiatry, Chosun University, 588 Seosukdong Dong-Gu, Gwangju City 501-717, Korea; Jae Min Kim, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize and discuss about predictors in male genital self-mutilation.

Summary:
Objective: This study was undertaken to identify the psychiatric aspects in patients with genital self-mutilation in Korea.
Method: The authors investigated sixteen cases in terms of general epidemiological characteristics, the nature of mutilation, diagnostic classification, mental status and psychopathology at the time of the act, psychodynamics of their behavior and risk factors.
Results: In terms of the mutilation types and instruments, transaction of penis type were committed most frequently(93.8%), mostly by knives(68.8%). Almost all of them felt comfortable after the act of self-mutilation(93.8%). The formal diagnoses of the subjects were mainly schizophrenia(87.5%). Major symptoms at the time of the act were delusion and/or hallucination(41.7%) and depressive state(29.2%). Psychodynamically, lots of cases could be explained as to punish failures in the male role(21.9%), related to religiosity (15.6%), and the wish to be or delusion of being female(12.5%).
Conclusions: The findings suggest that the risk factors for the genital self-mutilation are the deprivation of the early experiences, presence of psychotic disorder or depression, identity confusion, and the guilty feelings toward sexual aggression.

References:
NR133 Monday, May 3, 9:00 a.m.-10:30 a.m.
EEG Abnormalities Associated With Antidepressant Pharmacotherapy

Andrea Sterr, M.D., Psychiatry Department, LMU, Nussbaumstrasse E. 7, Munich 80336, Germany; Frank Padberg, M.D., Georg Juckel, Roland Margz, Ph.D., Ulrich Hegerl, Ph.D., Benedikt Amann, M.D., Oliver Pogarell, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize that mild EEG abnormalities may occur, but are generally rare under antidepressant monotherapy.

Summary:
Introduction: Epileptiform activity, intermittent slow waves, and other abnormalities in electroencephalography (EEG) may occasionally occur during treatment with classical or atypical antipsychotics. In contrast, limited data are available regarding adverse effects of antidepressants and recently EEG abnormalities have been reported after mirtazapine treatment. In this retrospective study, we investigated EEG changes in psychiatric patients receiving a stable monotherapy with mirtazapine, citalopram, reboxetine, venlafaxine or amitriptyline.

Methods: Digital EEG recordings of 255 patients were retrieved from a database and visually interpreted by two independent raters. Patient groups were defined by medication as follows: mirtazapine (n = 80), citalopram (n = 58), reboxetine (n = 22), venlafaxine (n = 50) and amitriptyline (n = 45).

Results: There were no statistically significant differences between groups regarding the frequency of EEG abnormalities (intermittent slow waves, slower posterior dominant rhythms and an exaggerated response to hyperventilation). EEG abnormalities were found in 6 patients with mirtazapine (7.5%), 4 with citalopram (6.9%), none with reboxetine, 9 with venlafaxine (18%) and 5 with amitriptyline (11.1%). Epileptiform activity was not observed in any group. Groups did not differ significantly in terms of demographic characteristics except for age.

Conclusions: Mildly abnormal EEG patterns may occur, but are generally rare during monotherapy with antidepressants.

References:

NR134 Monday, May 3, 9:00 a.m.-10:30 a.m.
Low Bone-Mineral-Density With the Use of Valproic Acid

Ayesha Waheed, M.D., Psychiatry Department, Penn State, 500 University Drive, Hershey, PA 17033; Paul A. Kettl, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to examine the prevalence of low bone mineral density in patients with chronic mental illness treated with Valproic Acid.

Summary:
Introduction: Use of Valproic acid has been linked with osteopenia and osteoporosis (1,2).

Method: A retrospective chart review of 35 patients chronically hospitalized who had received valproic acid for at least six months who also received a Dextra Scan was performed. Those with normal scan were compared to those with abnormal scan using chi square analyses.

Results: 60% of the patients on Valproic Acid showed osteopenia or osteoporosis on Dextra Scan. There was a tendency for patients with abnormal scan to be more often males (71% vs 43%, p=0.09), have a history of alcohol abuse (33% vs 21%, p=0.49), have a shorter length of stay (8.6 yrs vs 10.6 yrs, p=0.45) but it did not reach statistical significance. Patients with abnormal scan also had a lower BMI (23.3% vs 32.4%, p=0.001). There were no differences in average age or duration of illness. Approximately, 2/3 of both groups suffered from schizophrenia or schizoaffective disorder, and all patients were receiving other psychotropics. Interestingly, calcium and phosphorus were normal in all 25 patients in whom it was available. Osteoporosis was more likely to be seen in lumbar spine than in the femoral neck, and osteopenia was more likely to be seen in the right femoral neck than on the left or the lumbar spine.

Conclusion: Osteopenia is common in chronically ill patients treated with Valproic Acid. Normal calcium and phosphorus did not distinguish the groups. Dextra scan should be performed routinely in these patients.

References:
Results: Side effects, especially nausea, were more intense but roughly similar to those of the regular titration schedule. 3 patients had their atomoxetine discontinued, 2 patients decreased their dosage, while the others stayed at the same dose or a higher dose. 

Conclusions: The side effect profile of starting doses of 1.2mg/kg/d was acceptable in this population, although more severe than for the standard dose of 0.5mg/kg/d. There were no long-term effects of starting at the higher dose. These preliminary results, if confirmed, suggest that it may be worth the trade-off of greater side effects for a shorter stay.

References:


NR136 Monday, May 3, 9:00 a.m.-10:30 a.m.
Aripiprazole as an Augmentation Agent in Treatment-Resistant Depression Supported by Bristol-Meyers-Squibb

Louai A. Bilal, M.D., Department of Psychiatry, Thomas Jefferson University, 633 Chestnut East, Suite 210D, Philadelphia, PA 19107; Ashwin A. Patkar, M.D., Marja Mattila-Evenden, M.D., Kathleen S. Peindl, Ph.D., Kelly Stein-Marcus, Ph.D., Prakash S. Masand, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the possible therapeutic utility of adjunctive atypical antipsychotic agents in treatment-resistant depression

Summary:

Introduction/Hypothesis: Aripiprazole is a novel atypical antipsychotic with partial agonist activity at D2 and 5HT1A receptors and antagonism at the 5HT2 receptors. This study examined the clinical utility and tolerability of aripiprazole as an augmenting agent in patients with treatment-resistant depression.

Methods: In an open-label, rater-blinded, prospective study, 5 patients with major depression who had failed to respond to an adequate trial of at least one antidepressant were prescribed aripiprazole (dose 5-30 mg per day) for 6 weeks. The dose of pre-existing antidepressant remained unchanged during the study. Treatment response was defined as a 50% or greater reduction in scores on the Hamilton Depression Rating Scale (HAM-D) from baseline to end of treatment. Side effects were rated on the Simpson Angus Extrapyramidal Scale (SAES), the Barnes Akathisia Scale (BAS) and SAFTEE.

Results: The mean HAMD at baseline and end of treatment was 25.2 (8.58) and 4.67 (4.04), respectively. 4 out of 5 (80%) were responders. By end of second week the HAMD scores had reduced by 56%. The mean daily dose of aripiprazole was 12.5 mg. One patient developed akathisia. No subjects dropped out of the study due to side effects from aripiprazole. The common side effects reported were transient and mild akathisia: 2 out of 5 (40%) and aslight tremor: 1 out of 5 (20%).

Discussion/Conclusions: The study indicates the potential utility of aripiprazole as an augmenting agent in treatment resistant depression. Given the open-label design and the small sample size of the study, adequately powered, randomized, double-blind, placebo controlled trials are necessary to fully evaluate the role of aripiprazole in treatment-resistant depression.

References:


NR137 Monday, May 3, 9:00 a.m.-10:30 a.m.
Aripiprazole for Pediatric Bipolar Disorder: A Retrospective Chart Review

Melissa P. DelBello, M.D. Department of Psychiatry and Pediatrics, University of Cincinnati, College of Medicine, 231 Albert Sabin Way, PO Box 670559, Cincinnati, OH 45267-0559; Drew H. Barzman, M.D., Robert A. Kowatch, M.D., Elizabeth H. Gernert, B.S., Katherine B. Rappaport, M.D., Sergio Delgado, M.D., Sanjeev Pathak, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to: 1. Discuss the effectiveness of aripiprazole for the treatment of pediatric bipolar disorders; 2. Discuss the tolerability of aripiprazole for the treatment of pediatric bipolar disorders.

Summary:

Objective: The objective of this retrospective chart review was to evaluate the effectiveness and tolerability of aripiprazole for the treatment of children and adolescents with bipolar disorders.

Methods: The outpatient medical charts of 30 children and adolescents with a DSM-IV diagnosis of bipolar disorder, type I, II, NOS, or schizoaffective disorder, bipolar type were evaluated. The charts of outpatients treated with aripiprazole were reviewed by two child and adolescent psychiatrists who evaluated the severity and the improvement of the patients using the Clinical Global Impression (CGI) Severity and Improvement score and the Clinical Global Assessment Scale (CGAS).

Results: Patients were treated (mean duration 4 months ± 2.7) with aripiprazole at a mean starting dose of 9.3 mg ± 4.3 and a mean final dose of 10.3 mg ± 3.1. The overall response rate (defined by a CGI-improvement score of ≤ 2 at endpoint) was 67%. CGAS scores significantly improved from 48 ± 11 to 65 ± 11 (signed rank = 191, p <0.0001). No serious adverse events were identified on chart review. Common side effects were sedation (n = 10, 33%), akathisia (n = 7, 23%), and gastrointestinal disturbances (n = 2, 7%).

Conclusions: This retrospective chart review suggests that aripiprazole may be effective and well-tolerated for children and adolescents who have a bipolar disorder. Further controlled studies are necessary.

References:


NR138 Monday, May 3, 9:00 a.m.-10:30 a.m.
Antidepressant Augmentation With Open-Label Atomoxetine

Nada Milosavljevic, M.D., Psychiatry Department, Brown University, Butler Hospital, 345 Blackstone Boulevard,
Providence, RI 02906; Jordan M. Schecter, M.D., Lawrence H. Price, M.D., Linda L. Carpenter, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the potential utility of adding the selective norepinephrine reuptake inhibitor, atomoxetine, to standard pharmacotherapy regimen following nonresponse to an adequate antidepressant trial.

Summary:
Background: Atomoxetine is a selective norepinephrine reuptake inhibitor (SNRI) currently approved for treatment of ADHD. Other compounds that enhance synaptic norepinephrine, such as the tricyclic desipramine, have antidepressant effects. Reboxetine, a SNRI antidepressant available in Europe, has demonstrated efficacy both for monotherapy and as an augmentation agent. This case series study examined the role of atomoxetine for antidepressant augmentation.

Methods: Fifteen adult outpatients with primary major depressive disorder received open-label atomoxetine augmentation following partial- or nonresponse to an adequate trial (minimum 8 weeks) of standard antidepressant pharmacotherapy. Atomoxetine (40 mg q d) was added to ongoing medication regimens and titrated according to clinical response. Clinician- and patient-rated symptom assessments were completed at each clinic visit.

Results: Eleven (73%) patients completed a minimum of 6 weeks atomoxetine augmentation; 3 (20%) discontinued due to side effects. Mean±SD endpoint dose was 82±40 mg/d (range 25-120 mg/d). Nine patients (60%) met criteria for positive categorical response. Mean IDS-SR symptom scores decreased significantly from baseline to endpoint (t=4.0, p=.001), and mean clinician-ratings of social and occupational functioning increased (t=5.0, p=.0002). No vital sign or weight changes were detected, and the most common side effects were anxiety and nausea.

Conclusion: More studies are warranted to evaluate the potential utility of atomoxetine for antidepressant augmentation.

References:

NR139 Monday, May 3, 9:00 a.m.-10:30 a.m.
Effects of Repetitive Transcranial Magnetic Stimulation on Panic Attacks Induced by CCK-4 in Healthy Subjects
Frank Padberg, M.D., Psychiatry Department, CMU, Nussbaumstrasse 7, Munich 80336, Germany; Peter Zwanzger, M.D., Nikolas Volkel, M.D., Daniela Eser, M.D., Hans-Jurgen Moller, M.D., Robin Elia, M.D., Rainer Rupprecht, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize that rTMS does not affect experimentally induced panic with CCK-4 in healthy volunteers.

Summary:
Introduction: Preliminary findings suggest that low frequency rTMS may exert beneficial effects in patients with depression and anxiety disorders. To further explore its possible anxiolytic and antipanic properties we investigated the effects of rTMS treatment on experimentally induced panic in healthy subjects.

Methods: In a placebo-controlled cross-over design 11 healthy volunteers received a 1 Hz real or sham rTMS over the right dorsolateral prefrontal cortex (120% intensity related to the individual motor threshold, 1800 stimuli/day) on two separate days. Experimental panic induction with CCK-4 was carried out immediately after verum or placebo rTMS respectively. Panic symptoms were assessed using the API and PSS score.

Results: All subjects reported a marked panic response following CCK-4 administration after both verum and placebo treatment. ANOVA revealed no significant differences of the mean API- and PSS sumscores between both conditions.

Conclusions: In contrast to preliminary findings in patients with anxiety disorders low frequency rTMS did not affect experimentally induced panic with CCK-4 in healthy volunteers. However, our results add to other findings suggesting no influence of rTMS treatment on mood in healthy subjects.

References:

NR140 Monday, May 3, 9:00 a.m.-10:30 a.m.
Six-Month Outcome of Early Outpatient Treatment After Opioid Detoxification
Paolo Mannelli, M.D., Department of Psychiatry, Thomas Jefferson University, 833 Chestnut East, Suite 210E, Philadelphia, PA 19107; Charles C. Thornton, Ph.D., Edward Gotthell, M.D., Marvin Levine, M.A., Stephen P. Weinstein, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the importance of early treatment intervention and treatment evaluation in drug abuse.

Summary:
Introduction: Opioid detoxification is frequently characterized by poor long-term outcome and many patients relapse before post detoxification treatment is initiated. We investigated the 6-months outcomes of opioid dependent individuals entering an opiate-free outpatient treatment shortly after detoxification.

Method: Drug use, treatment and psychosocial variables were evaluated in 86 heroin abusers, using the Government Performance and Results Act (GPRA) Client Outcome Measures Form. Six months after engagement in a short term post-detoxification outpatient program results were compared with data from admission. Patients entered treatment within 1 day after discharge from detoxification and were referred to long-term programs upon completion.

Results: Significant reduction in drug (e.g. opioids p<.001) and needle use (p<.02) was recorded, together with less inpatient (p<.001) and more outpatient (p<.001) time spent in treatment. Employment increased (p<.003), while legal problems, related to drugs (p<.02) and as a total (p<.03), were decreased. Psychosocial changes were confirmed by examining the patients record of services. Improvement was not related to time spent in the post-detoxification treatment, or to its outcome, and subjects from the same detoxification program not entering treatment after discharge did not show a similar psychosocial improvement.
Conclusion: Early intervention after detoxification may be an effective adjuvant in the harm-reduction strategy for the treatment of opiate dependence.

References:

NR141 Monday, May 3, 9:00 a.m.-10:30 a.m.
Enhanced Creativity in Patients With Bipolar Disorder Compared With Caregivers
National Institute of Mental Health
Andrea M. Aiarcon, B.A., Department of Psychiatry, Stanford University, 401 Quarry Road, Room 2130, Stanford, CA 94305-5723; Natalie M. Baloga-Mintz, Stephanie Jaros, M.A., Deborah A. Perlick, Ph.D., Po W. Wang, M.D., Cecylia Nowakowska, M.D., Terence A. Ketter, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize that bipolar disorder patients compared to caregiver have enhanced creativity.

Summary:
Objective: To explore creativity and mood state in bipolar disorder patients (BD) compared to their caregivers (CG).
Method: Seventy-six BD and their 76 CG were assessed with the Barron-Welsh Art Scale (BWAS) and the Beck Depression Inventory (BDI).
Results: Overall, BD had significantly higher BWAS (18.0 ± 11.7) than CG (13.0 ± 8.8, p < 0.004), who were 7.3 years older (p<0.001). BD had significantly higher BDI (12.5±10.9) than CG (7.3±6.3, p<0.0005), and controlling for age, depression was associated with lower BWAS in CG but not BD. Twenty-nine BD with related CG had even higher BWAS scores (23.7 ± 12.4) compared to CG (12.9±8.3, p<0.003), who were 19.3 years older (p<0.0001). Forty-seven BD with unrelated CG had nonsignificantly higher BWAS (16.3±10.5) compared to CG (13.5±7.8), who had similar ages. BD with related CG had higher BWAS (p<0.001) and were 13.4 years younger (p<0.001) than BD with unrelated CG. CG related to patients had similar BWAS compared to CG not related to patients (p=NS), despite being 6.1 years older (p<0.03).
Conclusion: BD had enhanced creativity compared to their (older) CG, that was independent of degree of depression BD (but not CG). This was driven by patients with related (typically parental) CG. Age differences could confound these findings as BWAS generally decreased with age.

References:

NR142 Monday, May 3, 9:00 a.m.-10:30 a.m.
Anger Attacks in Depressed Inpatients: Evidence for a Male Depressive Syndrome
Dietmar Winkler, M.D., General Psychiatry, University of Vienna, Währinger Gürtel 18-20, Vienna 1090, Austria; Edda Pjrek, M.D., Siegfried Kasper, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize, that anger attacks seem to be more prevalent in male depressed patients.

Summary:
Objective: It has been proposed, that aggression plays an important role in the symptomatology of depression [1]. Furthermore it has been hypothesized, that this symptom is more prevalent in males than in females [2].
Methods: A follow-up study of 217 depressed patients (104 females, 113 males) previously treated as inpatients was performed using questionnaires. Study subjects were contacted after discharge from hospital by mail or phone. Overall response rate was 69.6%. Patients were asked to retrospectively rate their state during their last depressive episode. They had suffered significantly more often from anger attacks than female patients (1.21 ±2.97 versus 4.26±7.52 anger attacks per month; p=0.001). Anger attacks were characterized most frequently by palpitations (91.3%), agressive feelings (72.7%), dyspnea (71.7%), feeling of losing control (70.5%), panic (63.4%), hyperhidrosis (61.4%) and tremor (56.1%). 82.2% of patients had not had any anger attacks before, 78.7% regretted them afterwards.
Conclusions: Our findings are indicative of gender differences in regard to anger attacks in depression. Further study is required to replicate and extend our results to assess the significance of aggression as a gender-specific diagnostic criterion for depression.

References:
The study compared workers who accepted, considered, and declined referrals on the following: sociodemographics, disaster exposure, subjective distress, clinician-evaluated need, and interviewer seniority. Chi Square analyses failed to indicate significant differences among the three groups on sociodemographics, disaster exposure, or interviewer seniority. ANOVA indicated the three groups differed significantly on clinician-rated symptoms of PTSD and self-reported symptoms of PTSD, depression, and generalized distress ($p < .001$ for all analyses). Post-hoc analyses revealed that workers who accepted or considered referrals received more severe clinician ratings of PTSD symptoms than those who rejected referrals. Furthermore, workers who accepted referrals reported higher levels of PTSD, depression, or generalized distress than those who declined referrals. This suggests that disaster workers who accept psychotherapy referrals are those who are most distressed and underscores the value of making treatment available.

**References:**


**NR144**

**Monday, May 3, 9:00 a.m.-10:30 a.m.**

**Social Impairment and Mental Health Treatment Seeking in Primary Care**

**Supported by Eli Lilly and Company**

Marc J. Gameroff, Ph.D., CGEU - Unit 24, New York State Psychiatric Institute, 1051 Riverside Drive, New York, NY 10032; Mark Olsson, M.D., Myrna M. Weissman, Ph.D.

**Educational Objectives:**

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

- Characterize patterns of use and non-use of mental health services by a culturally heterogeneous, economically disadvantaged primary care population, and understand the unique impact of impaired social function on treatment seeking behavior.

**Summary:**

**Objective:** To determine the effect of impairment in social function on mental health treatment seeking by adult primary care patients.

**Method:** We analyzed cross-sectional data from a systematic sample of 997 adult patients attending an urban primary care clinic. Assessments were available in Spanish or English. Main outcome measures were level of impairment in social function assessed with items from the Sheehan Disability Scale; level and type of psychopathology assessed with the MDD, GAD, panic disorder, and substance use disorder modules of the PRIME-MD Patient Health Questionnaire, and the psychosis section of the Mini International Neuropsychiatric Interview; and whether patients had received mental health treatment in the past year.

**Results:** Only about half (52%) of all patients with moderate to extreme impairment in social function received mental health treatment during the past year. Compared to patients with no impairment, those with mild impairment were twice as likely to seek mental health treatment ($p = .003$; adjusted odds ratio [AOR] = 2.1, 95% confidence interval [CI] = 1.3-3.3), and those with marked or extreme impairment were nearly three times as likely to seek treatment ($p = .0007$; AOR = 2.9, 95% CI = 1.6-5.4). These results controlled for the presence of MDD, GAD, panic disorder, and psychotic symptoms, as well as age, race/ethnicity, employment status, recency of immigration, and level of social support.

**Conclusions:** In this primary care sample, impaired social function appears to be an independent catalyst for mental health treatment seeking, over and above common psychiatric disorders. By including an evaluation of social functioning in their assessment of mental health, primary care staff may be more likely to identify their patients in greatest need of mental health services.

**References:**

1. Mojtabai R, Olsson M, Mechanic D: Perceived need and help-seeking in adults with mood, anxiety, or substance use disorders. Arch Gen Psychiatry 2002; 59:77-84

**NR145**

**Monday, May 3, 9:00 a.m.-10:30 a.m.**

**Impact of Antipsychotics on the Use of Antiparkinson Agents Among Medicare Beneficiaries**

Juliette C. Taylor, Pharm.D., Pharmacy Department, University of Maryland, 12016 Montrose Village Terrace, Rockville, MD 208052; Nicole J. Brandt, Pharm.D., Becky Briesacher, Rhona Limcango, M.S.

**Educational Objectives:**

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

- Determine whether the use of antiparkinson agents have decreased in response to increased use of atypical antipsychotic agents in long-term care facilities;
- Describe the components and significance of the Medicare Beneficiary Survey dataset; and
- Describe the clinical implications of the observed prescribing trends.

**Summary:**

**Objective:** An advantage to using atypical antipsychotics is the decreased effect on extrapyramidal symptoms (EPS). This study will determine whether the use of antiparkinson agents has declined in response to increased use of atypical antipsychotics.

**Methods:** This retrospective analysis utilized the 1997-2000 Medicare Beneficiary Survey (MCBS). The MCBS is a nationally-representative dataset containing Medicare claims and detailed medical survey information on the institutionalized Medicare population. The sample was beneficiaries taking at least 1 antipsychotic during the year: approximately 2 million in nursing homes (NHs) and 660,000 in assisted living facilities (ALFs). The study examined monthly medication records for concomitant use of antiparkinson agents.

**Results:** Preliminary analyses found strong decreases in the use of antiparkinson medications among antipsychotic users in NH (10.5% in 1997, 11.7% in 1998, 9.9% in 1999, and 8.4% in 2000) but inconsistent trends in ALF (14.1% in 1997, 10.3% in 1998, 13.4% in 1999, and 10.5% in 2000).

**Conclusions:** This study is the first nationally representative picture of the concomitant use of antiparkinsonian and antipsychotic drugs in institutional settings. The decrease suggests a possible cost offset and risk reduction in polypharmacy associated with using atypical over conventional antipsychotics. Future work will analyze data from mental health facilities, examine claims records for Parkinsonian conditions, perform tests for significance, and isolate anticholinergic and dopaminergic antiparkinson agents.

**References:**

2. Briesacher B, Stuart B, Doshi J: Medication Use by Medicare Beneficiaries Living in Nursing Homes and Assisted Living Facilities. Report to DHHS, Office of Disability, Aging and Long-
NR146  Monday, May 3, 9:00 a.m.-10:30 a.m.
Do 23-Hour Beds Avert Hospitalization? An Analysis
Jocelyn Lluberes, M.D., Psychiatry Department, Temple University, 9231 Old Newtown Road, Philadelphia, PA 19115; Dhana Lakshmi Ramasamy, M.D., M.D., Ralph Spiga, Ph.D., William R. Dubin, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to: 1. Educate participants as to the role of a 23-hour bed level of care and enable them to identify patients that will benefit from a referral to this level of care; 2. Familiarize participants with the characteristics of patients that utilize 23-hour bed services.

Summary:
A twenty-three hour bed is a level of care that is used to treat, monitor and reassess patients with the goal of delaying a disposition until the clinical status is clarified. Managed care companies use this strategy to avert inappropriate acute psychiatric hospitalization. However, there is no data available to assess the effectiveness of this strategy. This paper assesses the outcome of 161 consecutive patients referred from a medical university inner city hospital psychiatric emergency service to 23-hour beds. Data collected includes patient demographic and epidemiological variables, clinical history and mental status evaluation. Almost 90% of patients referred to a 23-hour bed were dually diagnosed (mental illness and substance abuse). Disposition from the 23-hour bed was as follows: acute psychiatric hospitalization, 44%, subacute hospitalization, 24%, substance abuse rehabilitation program, 7%, detoxification unit, 4%, outpatient, 20% and data was not available for 1 patient. Outcomes were also evaluated for significant differences in demographic and epidemiological variables, clinical history, and mental status findings. Outcome data evaluating recidivism following the 23-hour bed disposition is also presented. Based on the findings of this study 23 hour beds do avert acute psychiatric hospitalization and redirect patients to more appropriate levels of care.

This is not a funded study.

References:

NR147  Monday, May 3, 9:00 a.m.-10:30 a.m.
Psychiatrist’s Attire: The Patient’s Perspective
Nikhil Nihalaini, M.D., Psychiatry Department, SUNY - Upstate, UMU, 750 East Adams Street, Syracuse, NY 13210; Arun Raj Kunwar, M.D., Jud Staller, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to understand the patient’s perceptions of how psychiatrists should dress and what is their attitude towards the traditional medical white coat.

Summary:
Objectives: To assess patient’s perceptions of how psychiatrists should dress and what is their attitude towards the traditional medical white coat.

Method: A voluntary/anonymous IRB approved survey consisting of seven questions was offered to all patients attending a university adult outpatient psychiatry clinic during a four week period in fall of 2003.

Results: Out of 63 subjects who responded, 52 were included in final analysis (remaining had incomplete answers). Majority (79%) of responders was female and majority (80%) was between the age of 20-50 years. 67% of the respondent thought that dress is an important part of a psychiatrist’s appearance. Most preferred dress for a male psychiatrist was “Casual pants and casual shirt” (by 75%) and for a female “dress shirt with pants/skirts” (by 71%). None of the subjects surveyed thought that psychiatrists should wear a white coat, in fact 50% thought that it has a bad influence on doctor-patient relationship. 17% of the patients thought their psychiatrist was not a medical doctor.

Conclusions: Patients prefer their psychiatrist to dress in “casual pants and casual shirts (male)/dress shirt with pants/skirts (female). Patients don’t want their psychiatrist to wear a white coat.

References:
References:

NR149  Monday, May 3, 9:00 a.m.-10:30 a.m.
Internet Health Information: Use and Psychological Coping
Joshua Fogel, Ph.D., Department of Mental Health, Johns Hopkins University, 624 North Broadway, Suite 861, Baltimore, MD 21205

Educational Objectives:
At the conclusion of this session, the participant should be able to understand the potential impact of Internet health information use in that it is not associated with psychological coping among those with breast cancer.

Summary:
Introduction/Hypothesis: Many individuals use the Internet to obtain health information regarding their illness. This study hypothesizes that greater Internet health information use among women with breast cancer is associated with increased psychological coping regarding their illness of breast cancer.

Methods: Cross-sectional survey design. Participants were all those from two breast surgeons practices in an out-patient medical setting. Survey response rate was 74.9% (n=188). All whites, African Americans, and Hispanic Americans were included (n=178). Questionnaires completed regarding Internet use and also coping as measured by the Brief Cope. The predictor was Internet use and the main outcome measure was the Brief Cope. MANOVA analyses were conducted for the 14 coping subscales. Following a significant MANOVA omnibus test, univariate ANOVA and multivariate ANCOVA analyses adjusting for covariates were performed.

Results: Univariate ANOVA showed acceptance, active coping, self-blame, and denial coping were associated with Internet use, but these results were not maintained in the multivariate ANCOVA models.

Conclusions/Discussion: Internet health information use is not associated with psychological coping in breast cancer patients. Clinicians may recommend Internet health information use among women who have no difficulties in daily activity and attendance of a one-time survey which assessed unsafe sexual practives and IH. The relationship between internalized homonegativity and sexual risk taking were analyzed.

Results: A one-way ANOVA comparing those who had and had not engaged in unprotected anal sex over 90 days prior to assessment showed that there was a significant mean difference on the IH scale, F=6.92, p<01, between these two groups.

Conclusion: The quantified relationship between increased internalized homonegativity and unsafe sexual behavior presents important clinical implications in the treatment of gay and lesbian populations as well as in HIV and STI prevention and treatment. Funding for this project was provided by the Centers for Disease Control (CDC).

References:

NR151  Monday, May 3, 9:00 a.m.-10:30 a.m.
The Relationship of Spiritual Well-Being, Anxiety, Depression, and Quality of Life in Active Old Age
Seungdeuk Cheung, M.D., Psychiatry Department, Yeunam University Hospital, Daemyung Dong Namgu, Daegu 705-717, South Korea; Jongbum Lee, M.D., Jinsung Kim, M.D., Wanseok Sec, M.D., Shinho Song, M.D., Eunjung Jung, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to understand the relationship between internalized homonegativity (IH) and unsafe sexual behavior in Men who have Sex with Men (MSM) as well as recognize the important clinical implications of IH as a mediator for STI and HIV infections in MSM.

Summary:
Previous research has identified internalized homonegativity in gay men and women as a correlate with indicators of psychological distress, such as depression, anxiety, or poor self-esteem. It has been hypothesized that internalized homonegativity is related to behaviors with important clinical consequences such as substance use and unsafe sexual behavior.

Objective: The aim of this study is to examine the relationship between internalized homonegativity and unsafe sexual behavior in a population of MSM.

Methods: Participants were 183 MSM from the New York City area who self-identified as sexually compulsive and completed a one-time survey which assessed unsafe sexual practives and IH. The relationship between internalized homonegativity and sexual risk taking were analyzed.

Results: A one-way ANOVA comparing those who had and had not engaged in unprotected anal sex over 90 days prior to assessment showed that there was a significant mean difference on the IH scale, F=6.92, p<01, between these two groups.

Conclusion: The quantified relationship between increased internalized homonegativity and unsafe sexual behavior presents important clinical implications in the treatment of gay and lesbian populations as well as in HIV and STI prevention and treatment. Funding for this project was provided by the Centers for Disease Control (CDC).

References:
of SWS. Satisfaction and feeling of life is related with significantly high score of SWS. These factors showed significant discriminative score of EWS rather than RWS. Compared with religion, SWS showed significant difference. Groups that have religion are related with significantly higher score of EWS and RWS than group that have no religion. Compared with satisfaction of religion, SWS showed significant difference. Assess the effect of SWB on anxiety, depression and quality of life by multiple regression analysis.

Score of SWS especially EWS effects on anxiety and depression of Korean Combined Anxiety and Depression Scale (CADS) significantly. Subjective feeling of life score is related with significantly low score of EWS and satisfaction of whole life score is related with significantly high score of EWS. In conclusion, SWB effects significantly on anxiety depression and quality of life in active old age, and we have a chance to verify spiritual well-being could be a new factor of health in old age.

References:

SR152  Monday, May 3, 9:00 a.m.-10:30 a.m.
Self-Hypnosis Techniques in the Clinical Practice
Elena Fernandez-Leon, M.D., La Paz University Hospital, Paseo de la Castellana 261, Madrid 28046, Spain; Ana Hospital, M.D., Ruth Berdun, M.D., Fabiola Irisarri, M.D., Marta Ramirez, M.D., Ignacio Millan, M.D., Marta Morales, M.D.

Educational Objectives:
At the completion of this session, the participant should be able to remark the usefulness of non pharmacological therapies in the pain treatment

Summary:

Objective: The purpose of this study was to examine the therapeutic applications of the hypnosis technique. The hypnosis, as a spontaneous phenomenon, is an attentive and receptive concentration condition that involves a relative suspension of the peripheral attention.

Method: A Likert Scale of the perceived improvement and evolution was administered to 9 patients who were referred from Oncology and Pain Department of La Paz University Hospital (February 2003). All participants had received treatment at the Psychiatry Department where Erickson's self-hypnosis techniques were implemented. In addition, referring department, reason for referral, social-demographic data, current physical and psychiatric history and type of treatment were reported. Mean differences on a Likert Scale before and after treatment as well as psychopathological evolution were examined.

Results: All participants had experimented anxiety disorders and the most common physical illness was fibromyalgia. The initial Likert's Scale average score was 9/10 and the patients who were treated with these techniques reported a 3 points average improvement.

Conclusion: These data show a subjective improvement in patients who had been trained in hypnosis techniques. This suggests that this treatment could reduce or avoid the use of ansiolytic drugs and also helps to improve patient's selfcontrol. Further research is needed in this field.

References:

SR153  Monday, May 3, 9:00 a.m.-10:30 a.m.
Methyltestosterone as an Adjunctive Treatment for Postmenopausal Depression
Rodrigo Dias, M.D., Psychiatry Department, Sao Paulo University, Rua Tabapua 821 Cj 55, Sao Paulo, SP 04533-013, Brazil; Florence Kerr-Correia, M.D., Luzia Trinca, Ph.D., Ricardo A. Moreno, M.D., Arlete Gianfaldoni, M.D., Anagloria Pontes, M.D., Hans Halbe, M.D.

Educational Objectives:
Objective: Androgens improve libido and cognition although there are few studies on depression. This study tries to evaluate HRT with and without androgens in menopausal depressive women.

Methods: Seventy two menopausal, depressive (DSM-IV) women, mean age 53.6 y.o., followed for 24 weeks were all treated with venlafaxine (37.5-225 mg/day) and double blind randomized into four HRT groups: G1) 20 patients - estrogen (0.625mg) plus medroxiprogesterone acetate (2.5mg) and methyltestosterone (2.5mg); G2) 20 patients - estrogen (0.625mg) plus medroxiprogesterone acetate (2.5mg) and methyltestosterone placebo; G3) 16 patients - estrogen placebo plus medroxiprogesterone acetate placebo and methyltestosterone placebo; and G4) 16 patients - estrogen placebo plus medroxiprogesterone acetate placebo and methyltestosterone placebo. Outcomes measured by Montgomery-Asberg Depression Rating Scale were analyzed by Repeated Measures Technique (MI and Mixed Procedures of SAS).

Results: At baseline, mean MADRS score was 30.72. No significant difference was observed between groups on drop-out rates (p=0.43). Statistical difference outcome among the groups was observed for MADRS score at the end of the study: p=0.034 - (G1: 4.46; G2: 7.01; G3: 5.51; G4:11.07).

Discussion: Results suggest better patient outcome with estrogen-androgens combination added to venlafaxine to treat postmenopausal women with depression.

References:
1. Soares CU, Poitras JR, Prouty J. Effect of Reproductive Hormones and Selective Estrogen Receptor Modulators on Mood During Menopause Drugs Aging 2003 20(2); 85-100

SR154  Monday, May 3, 9:00 a.m.-10:30 a.m.
Suicidal Ideation During Pregnancy
Lori C. Levey, M.S.W., Psychiatry Department, Emory University, 1365 Clifton Road, Building B, Suite 6100, Atlanta, GA 30322; D. Jeffrey Newport, M.D., Zachary N. Stowe, M.D.

Educational Objectives:
At the conclusion of this session, individuals will appreciate the degree of suicidal ideation in pregnant women and the best way to screen for it.

Summary:

Investigations have reported a lower rate of suicide during pregnancy compared to non-gravid populations. This raises questions: 1) Do pregnant women have the same incidence of suicidal ideation as non-gravid samples; 2) Does pregnancy protect against suicidal actions; and 3) Are self-rated scales adequate screening
tools in the obstetrical setting? Pregnant women (n=766) who presented to the Emory Women’s Mental Health Program were screened for inclusion in clinical research studies. Self-rated (Beck Depression Inventory [BDI]), Edinburgh Postnatal Depression Scale [EPDS]) and clinician-rated (Hamilton Rating Scale for Depression [HRSD]) depression questionnaires were obtained. Remarkably, 40% (305/766) of respondents reported thoughts of self-harm. In pregnant women who completed all scales (749/766), a total of 21% (155/749) endorsed thoughts of self-harm on all three scales. The rates of endorsement on the BDI and EPDS were 27% and 35%, respectively, compared to 28% on the HRSD. Additionally, 17% endorsed suicidal ideation only on the EPDS, and 9% endorsed only on the HRSD. These data suggest that the EPDS is the most conservative of the three scales, and is most likely to identify pregnant women with suicidal thoughts. It is noteworthy that none of the 305 women endorsing thoughts of self-harm attempted suicide while pregnant. Correlation between rating scale scores and use of scales in obstetrical clinics will be discussed.

References:

NR155 Monday, May 3, 9:00 a.m.-10:30 a.m.
Placental Passage of Tricyclic Antidepressants and Benzodiazepines
Ada M. Loughhead, B.S., Department of Psychiatry, Emory University, 1365 Clifton Road, Suite 6100, Atlanta, GA 30322; James C. Ritchie, Ph.D., Jeffrey Newport, M.D., C. Lindsay DeVane, Pharm.D., Jennifer L. Donovan, Ph.D., Zachary N. Stowe, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to understand SSRI clearance and dose management in pregnancy.

Summary:
Tricyclic antidepressants (TCAs) and benzodiazepines have been prescribed for decades and their safety in pregnancy continues to be controversial. It is remarkable that little is known regarding direct fetal exposure to these classes of medication. Twenty-one women taking TCAs and seventeen taking benzodiazepines participated in a study of the placental passage of medication. Maternal and umbilical cord blood pairs were collected at delivery. For women taking a TCA (clomipramine n=7; nortriptyline n=10), the mean ratio of umbilical cord to maternal sera concentrations (i.e. placental passage) was 0.7±0.4 for nortriptyline, and 1.4±2.4 for its ‘cis’ metabolite. The mean ratio of these pairs was 0.6±0.5 for clomipramine, and 0.8±0.6 for the metabolite. Eighteen pairs were collected from women taking a benzodiazepine (alprazolam n=2; clonazepam n=9; lorazepam n=7). The analyses and remaining assays are pending at time of submission. As a group TCAs and benzodiazepines did not demonstrate a difference in obstetrical criteria. Individual medication effects will be discussed. These data demonstrate variability in the individual of fetal exposure to medications of the same class, the limitations of ex vivo placental perfusion, and the need to measure active metabolites that may confer additional risks.

References:

NR156 Monday, May 3, 9:00 a.m.-10:30 a.m.
SSRI Clearance During Pregnancy: Clinical Implications
Autumn L. Henry, B.S., Emory University, 1365 Clifton Road NE, Suite 6100, Atlanta, GA 30322; D. Jeffrey Newport, M.D., James C. Ritchie, Ph.D., Zachary N. Stowe, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to understand SSRI clearance and dose management in pregnancy.

Summary:
There has been increased attention on antidepressants in pregnancy. The issue of reproductive safety has been extensively reviewed by survey groups. However, therapeutic monitoring guidelines during pregnancy and postpartum are sparse. One hundred and fifty-eight pregnant women treated with SSRIs were enrolled in the study. Maternal sera samples were collected at multiple gestational times in pregnancy (sertraline n=52, fluoxetine n=38, paroxetine n=28, venlafaxine n=20, citalopram n=15, escitalopram n=3, fluvoxamine n=2), and at least one time postpartum. Values were corrected for maternal daily dose. Preliminary data of fluoxetine clearance in pregnancy indicates a (n=4) mean ratio between 24 and 28 weeks gestation at 3.1±1.2ng/ml/mg drug. The mean ratio between 36 weeks gestation and delivery was 3.2±0.6ng/ml/mg drug. Serum concentrations dropped 30% in the second and third trimesters compared to the first trimester with a mean baseline of 4.4±1.4ng/ml/mg drug. The mean ratio of 5.7±0.7ng/ml/mg drug shows a dramatic rise in the postpartum period indicating that SSRI clearance and dose adjustment are necessary to decrease toxicity and side effects during pregnancy and postpartum. Additional analyses and remaining assays are pending at time of submission. Individual medication effects will be discussed.

References:
Summary:
The lifetime prevalence of anxiety disorders among women is estimated to be 30%. Studies of anxiety disorders during pregnancy are limited, but suggest an association between maternal stress and neonatal morbidity. The purpose of this study was to examine if anxiety in pregnancy is associated with adverse neonatal outcome.

Methods: We retrospectively reviewed clinical course in 1720 cases of pregnancy to investigate the prevalence of anxiety symptoms (generalized anxiety, panic, post-traumatic stress, or obsessive-compulsive).

Results: Prevalence of anxiety during pregnancy was 2.7% (47/1720). 19.1% (9/47) had no prior psychiatric history. Women with anxiety during pregnancy had a higher proportion of infants admitted to the neonatal intensive care unit (NICU) compared to women without anxiety (22.6% vs. 12.1%). Reasons for NICU admission included respiratory distress (n=2), prematurity (n=2), asphyxia (n=1), methadone withdrawal (n=1), and unknown (n=1). There were no differences in other neonatal outcome measures (gestational age, birth weight, 5 minute APGAR scores) between the two groups.

Conclusion: Prevalence of anxiety during pregnancy was lower than expected. Maternal anxiety during pregnancy was associated with greater rates of admission to the NICU compared to women without anxiety. Further study is needed to quantify the prevalence of anxiety disorders during pregnancy.

References:

NR158 Monday, May 3, 9:00 a.m.-10:30 a.m.
Validation of Psychometric Scales in Pregnancy
Kimberly A. Ragan, M.S.W., Department of Psychiatry, Emory University, 1365 Clifton Road, Suite 6100, Atlanta, GA 30322; D. Jeffrey Newport, M.D., Zachary N. Stowe, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to appreciate the impact pregnancy has on psychometric scales.

Summary:
To date, there is sparse validation of psychometric scales in pregnancy and their ability to discriminate between the symptoms of depression and the normal sequelae of pregnancy. A total of 365 pregnant women were screened for inclusion in clinical research. These subjects completed the Beck Depression Inventory (BDI), Dyadic Adjustment Scale (DAS), Perceived Stress Scale (PSS), and the clinician-rated 17-item Hamilton Rating Scale for Depression (HRSD-17) and Clinical Global Impression (CGI), range 1-7 with 1 being "not at all ill"). Preliminary analyses included pairwise comparison between CGI groups (ANOVA and Scheffé post hoc). Both the self-rated BDI and PSS, and the clinician-rated HRSD-17 significantly delineated both ends of the scale: CGI of 1-4 (M=118.18±13.5, M=113.56±15.9, M=109.28±19.2, M=108.80±14.7) were not significantly different from one another, however a trend toward an inverse relationship is evident. Further analyses including the impact of ethnicity and item factor analysis to determine a normative cutoff range for pregnancy and trimester-specific standard ranges for euthymia will be performed.

References:
D. Jeffrey Newport, M.D., Sarah E. Herbert, M.D., Angela F. Arnold, M.D., Zachary N. Stowe, M.D.

Educational Objectives:

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

1. Appreciate the complexity of reproductive safety data on antipsychotic medication.
2. Appreciate the multiple tiers of exposure and potential confounds in women with severe and persistent mental illness.

Summary:

The reproductive safety data for antipsychotic medications is limited. A total of sixty pregnant women (one set of twins) who had exposure to one or more antipsychotics in pregnancy were identified at the Women's Mental Health Program in Atlanta, Georgia (N = 60). Of the women identified, 77% were exposed to multiple psychotropics (polytherapy). Infants were first divided by monotherapy exposure vs. polytherapy exposure and then further divided by atypical, typical, or both types of antipsychotic exposure (Polytherapy: Atypical N = 15, Typical N = 18, Both N = 14, Monotherapy: Atypical N = 7, Typical N = 7). Means and standard deviations revealed no statistically significant differences within the two groups. The monotherapy group (N = 14) was then compared to the polytherapy group (N = 47) and again no statistically significant differences were found between weight (mean 2857 ± 1010, mean 3078 ± 725). Apgar 1, Apgar 5, gestation at delivery, delivery type and outcome. When weight of infants (N = 61) was compared to the 2001 Georgia Vital Statistics, a significant variance in proportion was found in extremely low birth weight infants <1499 (P = 0.001). Alcohol use was found in 20% of the women and 30% had other substance abuse. Smoking during pregnancy was identified in 38% of this population. Further analysis will look at comparisons between the antipsychotic group, diagnosis, and co-morbidity. The preliminary results underscore the limitation in attempting to assign risk of any adverse impact to an individual psychotropic medication.

References:


NR162  Monday, May 3, 1:00 p.m.-2:30 p.m.
Drug Company Funding of Clinical Psychiatric Research Related to Outcome

Robert Kelly, M.D., Psychiatry Department, Beth Israel, First Avenue at 16th Street, 6 Karpas, New York, NY 10003; Alison Bodenheimer, Elana Neustadtler, Arkady Barenboim, M.D., Lisa J. Cohen, Ph.D., Igor I. Galyenker, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be aware of mechanisms which can explain a possible association between pharmaceutical company funding of psychiatric treatment studies, and the outcomes of those studies.

Summary:

Introduction: This study examines the relationship between pharmaceutical company funding of psychiatric treatment studies and the outcomes of those studies.

Methods: The abstracts of all articles from 1992 and 2002 in the American Journal of Psychiatry (AJP) and Archives of General Psychiatry (AGP) were evaluated. Outcomes for drugs in articles not sponsored by drug companies were compared to outcomes in articles sponsored by drug companies, using a one-tailed Fisher's exact test. The proportion of articles sponsored by drug companies was also compared in 2002 vs. 1992, using a two-tailed Fisher's exact test.

Results: Positive outcomes were significantly more frequent in articles sponsored by the producers of the drugs in AGP (p = 0.03) and both journals combined (p = 0.02), but not in AJP (p = 0.15). A comparison of the proportion of articles sponsored by drug companies in 2002 vs. 1992 demonstrated a statistically significant increase for AJP articles (p = 0.006) and for both journals combined (p = 0.0002), but not for those in AGP alone (p = 0.07).

Conclusions: This study supports our hypothesis that positive outcomes are more frequent when pharmaceutical companies sponsor the research than when not. The data also indicate that over the last decade there may be a trend toward an increase in the proportion of psychiatric treatment studies sponsored by pharmaceutical companies.

References:

NR163  Monday, May 3, 1:00 p.m.-2:30 p.m.
Evidence-Based Side-Effect Tables of Anticonvulsants and Lithium: 2003 Update
T. Atilla Ceranoğlu, M.D., Psychiatry Department, Mass General Hospital, 72 Meadowbrook Road #4, Quincy, MA 02170; David N. Osser, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be more able to differentiate the side effect liabilities of anticonvulsant medications and lithium based on literature-based evidence. The participant should be able to compare these medications with similar indications and with placebo.

Summary:

Objective: Clinicians today are equipped with a far greater and improved armamentarium of medications to treat psychiatric disorders. It has become correspondingly difficult to choose the medication most likely to be well tolerated by the patient. Our objective is to construct quantitative, evidence-based side-effect tables for the medications used to treat depression and bipolar disorder.

Method: We reviewed double blind randomized clinical trials published in psychiatry and neurology literature before May 2003 and pooled the available data on important side effects. Weighted percentages were entered into tables and compared.

Conclusion: Carbamazepine and gabapentin appear to produce CNS side effects less commonly while oxcarbazepine, Lithium and topiramate seem to cause higher incidence of CNS symptoms. Lamotrigine is associated with more frequent rash but less frequent GI side effects. Valproic acid was found to produce fewer headaches than placebo, but GI symptoms and alopecia are problematic. Lithium has a high incidence of GI side effects. The meta-analysis was limited by many inconsistencies in the way adverse events are reported in research. Despite the limitations, this analysis represents the most accurate quantitative evidence-based review of the side effects of these medications and contrasts with the usual side effect table where rates are based on the author’s experience as 1+, 2+, etc.

References:


NR164  Monday, May 3, 1:00 p.m.-2:30 p.m.
The Application of Evidence-Based Care in PTSD
Lorna K. Mayo, M.D., Psychiatry Department, Dartmouth Medical University, One Medical Center Drive, Lebanon, NH 03756; Bradley V. Watts, M.D., David H. Rubin, M.D., Rebecca L. Hirsch, M.D., Keith R. Warren, M.D., Bradley McClure, M.D., Naomi M. Mendelovicz, M.D.

Educational Objectives:

At the conclusion of the session participants should demonstrate an understanding of the use of evidenced-based practice for PTSD in a clinical population, and develop an awareness of the possible implications.

Summary:

Objective: There are demonstrated efficacious treatments for post-traumatic stress disorder (PTSD). These include specific medications and psychotherapy. There is little information about how often these evidence-based practices are provided to patients. The purpose of this study is to determine how often the evidence-based treatments are provided.

Method: A retrospective chart review was performed of the 982 patients treated for PTSD at the outpatient mental health clinic at the White River Junction VA Medical Center in 2001. Medication trials and number of individual and group psychotherapy sessions were obtained.

Results: Of the 982 outpatients treated in for PTSD, 14% received a trial of sertraline, 9% a trial of paroxetine, and 32% a trial of any selective serotonin reuptake inhibitor. Patients averaged 3.4 individual psychotherapy sessions (range 0-53) and 4.5 group psychotherapy sessions (range 0-166). Eleven percent of patients had at least 10 individual sessions, and 13% had at least 10 group therapy sessions. Only 44% had a trial of either an SSRI or ten sessions of individual or group therapy.

Conclusions: Only about half of patients treated for PTSD in this VA outpatient sample during 2001 received a trial of any of the evidence based treatments for PTSD.

References:


NR165  Monday, May 3, 1:00 p.m.-2:30 p.m.
Funding Source, Outcome, and Quality of Bipolar Disorder Drugs Reports
Federico Soldani, M.D., Department of Psychiatry, Harvard Medical School, McLean Division of Massachusetts General Hospital, 115 Mill Street, Belmont, MA 02478; S. Nassir Ghaemi, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to assess the relation between funding source, study outcome and methodological quality of recent drug treatment reports on bipolar disorder.

Summary:

Method: A random sample of drug treatment studies (1998-2002) was identified by MEDLINE and PsyclNFO searches in 5 psychiatric journals with the highest ISI Impact-Factors. Funding sources and study outcome were assessed as reported in print; methodological quality evaluated according to study design (5 levels-of-evidence), conclusions based on p-values (i.e. a confounded measure), assessment of precision (confidence-intervals or power-analysis), loss-to-follow-up, citation of methodological references.

Results: We obtained a representative sample of 22 original articles (sampling fraction =0.17). 7/7 sponsored by pharmaceutical companies presented favorable results for the drug vs. 7/15 with other or no funding declared (RR 2.14; 95%CI 1.25-3.68). 2/7 vs. 3/15 had a randomized design (1.43; 0.30-6.72). Among 13 prospective studies, 3/6 vs. 6/7 had a drop-out rate >40% (0.58; 0.25-1.37). 2/7 vs. 5/15 had references about design or statistical methods (0.86; 0.22-3.38). Only 3 studies addressed precision, all not pharmaceutically funded, while virtually every report based at least part of the conclusions on p-values.

Conclusions: Pharmaceutically funded studies tend to have a randomized design and lower drop-out rates but seem less likely to address precision. There is a clear association between pharmaceutical sponsoring and the publishing of results favorable to experimental drugs. Possible explanations include a more careful
selection of which studies get funded, lack of an appropriate comparator or dosage, and publication bias.

References:

NR166 Monday, May 3, 1:00 p.m.-2:30 p.m.
Effects of Atypical and Typical Neuroleptics on ACC Volume in Schizophrenia
Laurie M. McCormick, M.D., Psychiatry Department, University of Iowa, 206 Hawkins Drive, 278W GH, Iowa City, IA 52242; Lawrence Decker, Peg Nopoulos, M.D., Nancy C. Andreasen, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to better understood the effects of atypical and typical neuroleptics or anterior cingulate cortex (ACC) volume in relation to gender and laterality differences and its relation to clinical outcomes.

Summary:
Objective: To investigate the effects of atypical versus typical neuroleptics on anterior cingulate cortex (ACC) volume over time and how it relates to the clinical outcomes.
Method: The sample was comprised of 29 patients meeting DSM-IV criteria for schizophrenia and 18 age-matched normal controls. Subjects were studied in a prospective longitudinal design, with MRI and comprehensive structural assessments at baseline and after 2-5 years. Patients were divided into typical or atypical neuroleptic exposure groups and the effects of age, gender, and dose-years were assessed in relation to ACC volume change. The effects of olanzapine versus risperidone were also evaluated as were clinical symptoms.
Results: Decreased ACC volume was significantly related to exposure of atypicals, whereas increased ACC volume was associated with exposure to the typicals over time. Decreased left ACC volume was associated with females on risperidone, whereas increased left ACC volume related to males on typicals. There was a correlation between improved psychotic symptoms and increased left ACC volume in males on typicals, although both neuroleptic groups showed improvement in clinical symptoms.
Conclusions: These results suggest that atypical and typical neuroleptics are associated with changes in ACC volume over time that differs for males and females.

References:

NR167 Monday, May 3, 1:00 p.m.-2:30 p.m.
Quantitative Measures of White-Matter Diffusivity in Manic Adolescents
John N. Adams, B.S., Psychiatry Department, University of Cincinnati, 231 Albert Sabin Way, Cincinnati, OH 45267-0558; Caleb M. Adler, M.D., Melissa P. DelBello, M.D., Neil P. Mills, B.S., Stephen M. Strakowski, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able:
1. Identify white matter abnormalities in manic adolescence; 2. Describe how diffusion tensor imaging in patients with bipolar disorder may be useful for bipolar-patients.

Summary:
Objectives: Several lines of evidence suggest that affective and cognitive findings in bipolar disorder may be related to a dysconnectivity syndrome involving white matter pathology. Previous studies utilized diffusion tensor imaging to observe subtle white matter changes in patients with bipolar disorder. These studies suggested white matter changes are developmental in nature. We hypothesized that subtle white matter changes may be present in adolescent patients with bipolar I disorder.
Methods: 12-18 year-old adolescent patients (N=21), characterized as either first manic episode (N=13) or multiple episode (N=8), and 10-18 year-old healthy controls (N=17) were recruited. DTI and localizing anatomic data were acquired, and regions-of-interest (ROIs) identified. Fractional anisotropy (FA) and trace apparent diffusion coefficient (TADC) were compared by ROI between study groups.
Results: Adolescent patients with bipolar disorder showed changes in measures of white matter integrity in several brain regions. These changes were unrelated to age and gender. Follow-up analysis suggests that changes were present in even first-episode patients.
Conclusions: Our findings suggest that a loss of white matter integrity is present in adolescent patients with bipolar I disorder, early in the course of their illness. Moreover, the developmental nature of white matter changes in adolescence may have pathological significance related to bipolar I disorder.

References:

NR168 Monday, May 3, 1:00 p.m.-2:30 p.m.
Association Between the Val66Met Variation in the BDNF Gene and Bipolar Disorder: A Replication Study
Falk W. Lohoff, M.D., Psychiatry Department, University of Pennsylvania, 526 Spruce Street, Philadelphia, PA 19106; Thomas Sander, M.D., Jurgen Gallinat, M.D., Wade H. Berrettini, M.D.

Educational Objectives:
Objective: Recent studies have indicated that the brain-derived neurotrophic factor (BDNF) gene is involved in the etiology of bipolar disorder (BPD). The BDNF gene maps to chromosome 11p13, a region where linkage studies have suggested a putative locus for BPD. Two family based association studies showed that the functional polymorphism Val66Met in the BDNF gene is associated with BPD, however others could not confirm results. Here we perform a replication study in an independent sample and test the hypothesis that the Val66Met variation in the BDNF gene confers susceptibility to BPD.
Methods: Genotypes of the Val66Met variation were obtained in 345 bipolar patients and 998 healthy controls, using Applied
Reduced Cortical Folding in Individuals at High Risk for Schizophrenia

Roger J. Jou, M.D., Psychiatry Department, University of Pittsburgh, P.O. Box 42316, Pittsburgh, PA 15203-0316; Antonio Hardan, M.D., Matcheri S. Keshavan, M.D.

Educational Objectives:
- At the conclusion of this session, the participant should be able to: 1) Appreciate the significance of cortical gyriﬁcation in understanding the pathophysiology of neuropsychiatric disorders; 2) Understand the possible implications of abnormal cortical gyriﬁcation in individuals at high risk for developing schizophrenia; 3) Identify the limitations of the current study and interpret its results in the context of those limitations.

Summary:
- Objective: The gyriﬁcation index (Gl), the total cortical contour divided by the outer contour, is a measure of cerebral cortical folding. Studies have documented its reduction in individuals with schizophrenia, and this investigation attempts to examine the gyriﬁcation pattern in individuals at high risk for developing schizophrenia.
- Method: Using MRI scans and the Brains2 software, Gls were calculated for 17 high-risk adolescents (at least one ﬁrst-degree relative with schizophrenia) and 15 controls (no family history of schizophrenia). Using the coronal slice just anterior to the corpus callosum, the total and outer contours were manually traced to allow calculation of the Gl.
- Results: There were no signiﬁcant differences in gender composition (high-risk: 10 males, 7 females; control: 13 males, 2 females) or age (high-risk=15.2±3.0 years; control=14.5±5.4 years). The left Gl was lower in the high-risk group when compared to controls (high-risk=2.95±0.30; control=3.21±0.35; t=2.19, df=30, p=0.036). However, no difference in the right Gl was observed between these two groups (high-risk=3.03±0.35; control=3.11±0.24; t=0.746, df=30, p=0.461).
- Conclusions: These results suggest reduced cortical gyriﬁcation in the left frontal lobes of persons at high risk for schizophrenia. This ﬁnding is consistent with studies of schizophrenic patients and supports genetic and neurodevelopmental models of the disorder.

References:

NR170 Monday, May 3, 1:00 p.m.-2:30 p.m.
Regional Cerebral Perfusion Abnormalities in Tic Disorder
Jaein Lim, M.D., Department of Psychiatry, Seoul National University, 28 Yeongdongdong Chongnogu, Seoul 110-744, South Korea; Hyunju Seo, M.D., Kanguei Hong, M.D., Bungnyun Kim, M.D., Soochurl Cho, M.D., Minseop Shin, Ph.D.

Educational Objectives:
- The conclusion of this session, the participants can recognize the abnormal cerebral perfusion areas in Tic disorder and its relationship with known pathophysiology of Tic disorder.

Summary:
- Objective: An investigation of cerebral blood ﬂow using Tc-99m-HMPAO brain SPECT was conducted to identify functional abnormality of the brain of tic disorder.
- Method: Twenty-one patients with chronic tic or Tourette’s disorder who had no previous treatment history were selected by using DSM-IV criteria.(M:F=19:2, 9.73±2.11y) After acquiring a pre-treatment Tc-99m-HMPAO Brain SPECT Images from them, Statistical Parametric Mapping analysis was performed by using standard template of child-adolescent normal control.
- Result: Decreased cerebral blood ﬂow in both medial frontal gyrus, left paracentral lobe, left precuneous gyrus were found in tic disorder group compared to the controls.(P<0.001) In addition, increased blood ﬂow in both inferior, middle, superior frontal gyri were found in tic disorder group.(P<0.001)
- Conclusion: A signiﬁcant cerebral blood ﬂow abnormality in frontal lobe of tic disorder in our study suggests an association with the previously known abnormality in circuit of fronto-striato-thalamo-frontal area. Decreased blood ﬂow areas are partially in accordance with known blood ﬂow reduction in left hemisphere.

References:

NR171 Monday, May 3, 1:00 p.m.-2:30 p.m.
Forty-Year Validation of Nine Methods of Defining Familial Alcoholism
Sreelatha Spieker, M.D., Psychiatry Department, Kansas University Medical Center, 3901 Rainbow Blvd #1009 Olath, Kansas City, KS 66160; Bjorn Edbrup, B.M.D., Elizabeth C. Penick, Ph.D., Elizabeth J. Nickel, M.A., Joachim Knop, M.D., Per Jensen, M.D., William F. Gabrielli, Jr., M.D.

Educational Objectives:
- At the conclusion of this session, the participant should be able to compare the accuracy of nine definitions of familial alcoholism in predicting drinking and non-drinking outcomes at age 40 years.
Summary:

Objective: Utilize data generated from a Danish birth cohort formed in the late 1950's to compare the long-term clinical validity of nine different methods of defining familial alcoholism.

Method: This high risk, longitudinal study of a group of sons of alcoholic fathers and sons of non-alcoholic fathers (N=330) were comprehensively studied at birth, at age one year, at 19-20 years, at 30 years and now finally at 40 years. The 40-year follow-up included 67 percent of the original sample, including the 21 who had died (N=201). Six of the 9 methods of defining familial alcoholism were based upon the family history method (subject report at age 30) that ranged from simple to complex; two methods were based on Danish national archival data only; and 1 method was based upon a combination of family history and archival data. Current and lifetime measures included historical information, quantity/frequency of drinking, alcoholism severity, common sequelae of abusive drinking and other indices of psychosocial functioning over time.

Results: All nine methods were significantly correlated with each other. All nine methods post-dicted or predicted at least some of the a priori validity measures. Archival methods were least effective in predicting 40-year outcomes; family history methods were most predictive.

Conclusion: The most valid methods of defining familial alcoholism were also among the most easy to implement in clinical settings.

References:

NR172 Monday, May 3, 1:00 p.m.-2:30 p.m.
Depressive Symptoms and Suicidal Ideation Among College Students
Shamsah B. Sonawalla, M.D., Department of Psychiatry, Massachusetts General Hospital, 50 Staniford Street, Suite 401, Boston, MA 02114; Erin C. Beaumont, B.A., Yasmin Mahal, B.A., Dan V. Iosifescu, M.D., David Mischoulon, M.D., Jonathan E. Alpert, M.D., Maurizio Fava, M.D.

Educational Objectives:
- At the conclusion of this presentation, the participant should be able to: 1) recognize that depression and suicidal ideation are prevalent among college students; 2) understand that it is important to screen for depression and plan effective intervention strategies in this population

Summary:
- Objective: To assess the prevalence of depressive symptoms and suicidal ideation among college students.
- Method: 752 students at a college in the greater Boston area (mean age: 20.2 years ± 7.6 years; 59.3% women) were screened for depressive symptoms. After obtaining written, informed consent, the Beck Depression Inventory (BDI) was distributed to all students. Students who scored greater than or equal to 16 on the BDI and consented to be interviewed were evaluated using the MDD module of the Structured Clinical Interview for DSM-IV (SCID-P). Students who met criteria for MDD on the SCID were examined for evidence of substance use disorder and depression severity was measured using the Beck Depression Inventory (BDI). Subjects who scored > 16 on the BDI were further assessed using the 10-item Harvard Department of Psychiatry/National Depression Screening Day scale (HANDS) and a questionnaire. For the purpose of the analyses, significant depressive symptoms were defined as a score of ≥ 10 on the BDI.

Results: Nineteen percent of the students had significant depressive symptoms, as assessed by a score of ≥ 10 on the BDI, and 7.3% of the students scored ≥ 16 on the BDI. 14.4% of the students reported suicidal ideation (score of ≥1 on BDI item #9). Age, gender and year in college did not predict suicidal ideation. Depression severity predicted suicidal ideation (P<0.0001). Women were significantly more likely to have a total BDI score ≥ 10 compared to men (22.4 % vs 14.0%; chi-square = 8.3; P < 0.01). 30% of the students reported sleep disturbances, as assessed by a score of ≥1 (item # 16) on the BDI. Students who reported sleep disturbances were significantly more likely to have suicidal ideation, compared to those who did not (20% vs 11.9% respectively; chi-square - 8.5; P<0.01).

Conclusion: A substantial percentage of students in this sample reported experiencing significant depressive symptoms, suicidal ideation and sleep disturbances. More women than men experienced significant depressive symptoms. This study highlights the importance of screening for depressive symptoms in college populations, and suggests that depressive symptoms may vary with gender.

References:

NR173 Monday, May 3, 1:00 p.m.-2:30 p.m.
Temperament and Character Patterns of Internet Game Addictions in Adolescents
Bong Ki Son, M.D., Psychiatry Department, Hallym University, Kyo dong, Sacred Heart Hospital, Chunghun 200-704, South Korea; Hong Seock Lee, M.D., Sang Kyu Lee, M.D.

Educational Objectives:
- At the conclusion of this presentation, the participant should be able to recognize the temperament and character patterns of internet game addiction in adolescents and the differences of internet game addiction from other addictions in TCI.

Summary:
- Objective: The purposes of this study were to investigate the temperaments and character patterns of internet game addiction in the Korean high school students and to compare with other substance addictions.

Method: Subjects were 482 high school students (male/female= 245/237) who resided in urban area. All subjects were given the questionnaires, which included Computer Game Addiction Test (GAT), Temperament Character Inventory (TCI) and the history of experiencing the alcohol or smoking. The GAT for the Koreans was revised from the Young's Internet Addiction Test and it was found to be reliable (Cronbach's alpha=0.88). When subjects answered "yes" in more than 10 items of GAT, we put them in "high risk", and when less than 10, in "low risk".

Results: 172(36%) subjects were in the high risk group. According to the results of TCI, the high risk group showed higher scores in 'harm avoidance', 'self-transcendence' and lower 'reward dependence', 'self-directedness', 'cooperativeness' than the low risk. But subjects with alcohol or smoking had higher 'novelty seeking' but 'harm avoidance' score was lower only in subjects experienced smoking than non-experienced.
Conclusions: It has been suggested consistently that the addicted persons showed high 'novelty seeking' scores, low 'harm avoidance' and 'self-directedness' scores. This study revealed that the pathophysiology of game addiction in adolescents might be different from other addictions.

References:

NR174 Monday, May 3, 1:00 p.m.-2:30 p.m.
Comparative Prevalence of Depression by Race/Ethnicity: Findings From the Third National Health and Nutrition Examination Survey (NHANES)

Tuananh Nguyen, M.D., Psychiatry Department, University of Michigan, 2101 Commonwealth, Suite C, Ann Arbor, MI 48105; Stephanie Riolo, M.D., Christen Flack, Cheryl King, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able:
(1) gain knowledge regarding the epidemiology of depression by subtypes; (2) Identify factors that contribute to racial/ethnic differences in depression prevalence.

Summary:
Objective: To examine prevalence of different types of depression by race/ethnicity, controlling for age, gender, education, and income, using the findings from the third National Health and Nutrition Examination Survey (NHANES III).

Method: Data were collected in a nationally representative survey conducted from 1988-1994. African Americans and Mexican Americans were oversampled to obtain more reliable estimates. The diagnostic interview schedule (DIS) was administered to 8,449 participants (15-40 years), allowing diagnosis using DSM III-R criteria.

Results: Prevalence of Major Depressive Disorder (MDD) is statistically greater (P=0.03) in whites (10.4%) versus African Americans (7.5%) and Mexican Americans (8%). By contrast, prevalence of Dysthymic Disorder (DD) is more common (P=0.05) in African Americans (7.5%) and Mexican Americans (7.4%) versus whites (5.7%). Recurrent spells of depression are more common (P=0.003) in whites (18.2%) versus African Americans (13.3%) and Mexican Americans (12.9%). These differences remain significant even after controlling for age, gender, and education.

Conclusion: The findings of this study are very important and confirm what others (Robins; Jackson) have suggested previously - that comparative prevalence of depression by race/ethnicity depends on the type of depression. The quality and size of the NHANES III sample allows subgroup analyses revealing high risk subgroups.

References:

NR175 Monday, May 3, 1:00 p.m.-3:00 p.m.
A Ten-Year Follow-Up of Early-Onset Alcoholics With and Without Antisocial Personality Disorder

Ashley W. Walters, M.D., Psychiatry Department, Kansas University Medical Center, 3901 Rainbow Boulevard, Kansas City, KS 66160; Elizabeth C. Penick, Ph.D., Elizabeth J. Nickel, M.A., Barbara J. Powell, Ph.D., Jan L. Campbell, M.D., Barry I. Liskow, M.D., Edward N. Hunter, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to:
(1) recognize associations between substance use, gender and personality disorders; (2) demonstrate that male gender and use of multiple substances is connected to the diagnosis of antiso-
comorbid personality disorder; (3) and discuss personality clusters among pure alcoholics versus other substance users.

Summary:

Background: A study by Landheim, Bakken and Vaglum published in January of 2003 concludes that male polysubstance users more often presented with antisocial personality disorder; furthermore, female pure alcoholics more often had Cluster C personality disorders than other substance users, while male pure alcoholics presented with Cluster A personality disorders more often. Earlier studies had not shown these associations.

Objective: This study attempts to reproduce the results of the study by Landheim, Bakken, and Vaglum.

Method: Charts of patients presenting to the inpatient substance rehabilitation program from May 2002 to May 2003 at Bergen Regional Medical Center were retrospectively reviewed for Axis I diagnosis of substance dependence Axis II diagnosis, and gender. P values for differences between percentages were calculated.

Results: Among 41 patients with Axis I diagnosis of substance dependence and Axis II diagnosis of personality disorder, 33% of pure alcoholics vs 67% of alcohol plus other substance(s) users had the diagnosis of antisocial personality disorder (P<0.036). Among patients diagnosed with antisocial personality disorder, 11% were female and 89% were male (P<0.001). Male pure alcoholics presented with Cluster A personality disorders more often than other substance users (30%) while female pure alcoholics more often had Cluster C disorders than other substance users (22%).

Conclusion: This study confirms conclusions of the Norwegian study by Landheim, Bakken and Vaglum.

References:

NR177 Monday, May 3, 3:00 p.m.-5:00 p.m.
Atypical Antipsychotics and Schizophrenia With Comorbid Substance Abuse
John E. Zeber, M.H.A., HSRD, Veterans Affairs, 928 Rose Drive, Ann Arbor, MI 48103; Laurel Copeland, Ph.D., Frederic C. Blow, Ph.D., David A. Smelson, Psy.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to appreciate the complex challenge of treating dual diagnosis patients and to recognize the additional benefits of atypical antipsychotics for individuals with schizophrenia and comorbid substance abuse.

Summary:
Objectives: Veterans with schizophrenia and drug dependency are less stable in terms of medication utilization and compliance compared with similar patients without substance abuse. However, atypical antipsychotics (AP) may stabilize dopamine levels, diminish cravings, and are more efficacious than conventional drugs.

Methods: National Psychosis Registry data for FY99 yielded AP prescriptions and compliance among 58,816 veterans with and without substance abuse (cocaine/alcohol dependence). Then, among dual-diagnosis veterans, we examined differential effects of atypical or conventional APs on utilization, compliance, and relapse (re-admission <90 days). Results: 14% of patients were diagnosed with schizophrenia and comorbid dependence. Compared with patients with schizophrenia alone, dually diagnosed veterans received more multiple APs (37% vs. 25%), were twice as noncompliant, and used more health care services. They also more commonly received atypical APs (70% vs. 55%). Atypicals were not associated with decreased inpatient use; however, noncompliance rates were significantly lower (multivariate OR=.82). Conclusions: Compared with conventional APs, atypical agents appear to offer significant benefits for vulnerable, high-utilization, dual-diagnosis patients. Atypicals may improve compliance, relieve substance abuse cravings, and potentially reduce psychiatric admissions. Further research should examine atypicals and symptomology, focusing on illness burden from both schizophrenia and addiction.

Funding Source(s): Veterans Affairs HSRD
References:

NR178 Monday, May 3, 3:00 p.m.-5:00 p.m.
Seasonal Variation in Mood and Behavior in Romanian Postgraduate Students
Samina M. Youssufi, M.D., Department of Psychopharmacology, St. Elizabeths Hospital, 2700 Martin Luther King Jr. Avenue, Washington, DC 20032; Constantin Ciupagea, Ph.D., Kelly J. Rohan, Ph.D., Dorin B. Neculai, M.D., Ryszard Zebrak, M.D., Teodor T. Postolache, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the pattern of seasonality in Romanian students. Despite Romania hot summers and the relative unavailability of air conditioning as compared with the other Caucasian nations, their winter SAD prevalence may be related to the genetic and/or ethnic and/or latitude interaction.

Summary:
Objective: We hypothesized that winter SAD would be more prevalent than summer SAD in Romanian college students, even if in Romania summers are hot in comparison with Scandinavian countries and the air conditioning relatively unavailable in comparison with the U.S.

Method: A convenience sample of 488 postgraduate students, completed the Seasonal Pattern Assessment Questionnaire (SPAQ), which was used to calculate a global seasonality score (GSS), and estimate the prevalence of winter- and summer-type SAD. The prevalence of summer vs. winter pattern of seasonality of SAD was compared using multinomial probability distribution tests.

Results: Out of 488 students who were invited to participate, 476 returned the completed questionnaires. Winter SAD and winter subseasonal SAD (ssSAD), was significantly more prevalent than summer SAD (p<0.038) and summer ssSAD (p < 0.006). Mean global seasonality score (GSS) was 7.58.

Conclusions: Our results are consistent the prevalence and pattern of SAD previously reported across countries with cooler summers or controlled summer microclimates.
NR179  Monday, May 3, 3:00 p.m.–5:00 p.m.
Adjunctive Tiagabine for Treatment-Refractory Social Anxiety Disorder

Gustavo D. Kinrys, M.D., Psychiatry Department, Cambridge Hospital, 1493 Cambridge Street, Cambridge, MA 02139; Federico Soldani, M.D., Douglas J. Hsu, B.S., Tamara B. Pardo, B.A., Maria Melo, B.A., John J. Worthington III, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to appreciate the potential efficacy of adjunctive tiagabine treatment in SAD patients.

Summary:
Objective: Social anxiety disorder (SAD) is the third most common psychiatric disorder, with a lifetime prevalence of 13.3% in the United States. The costs associated with SAD are considerable, with associated increased physical and emotional health difficulties, alcohol abuse, and high rates of psychiatric comorbidity. Many patients remain symptomatic despite initial intervention. We examined the acute and long-term efficacy and safety of adjunctive tiagabine in 12 patients with generalized SAD.

Method: Retrospective analysis of a cohort of patients with SAD (N=12), with partial or non-response to SSRIs, that received adjunctive tiagabine for at least 28 weeks in a naturalistic fashion.

Results: Patients improved significantly on all measures (Endpoint LSAS: 44.25±21.23, 95%CI 22.87–57.46, p<0.0001; CGI-S: 3.0±1.7, 95%CI 1.39–4.10, p<0.0001), with a mean decrease in LSAS of 40 points. Most patients (58.3% or 7/12) met responder criteria at endpoint (CGI-I<2) and 41.6% (5/12) met remission criteria in LSAS of 40 points. Most patients (58.3% or 7/12) met responder criteria why they had been restrained. Most thought that restraint had been unnecessary. Being restrained evoked feelings of anxiety, anger, and hostility. Some calmed down in restrains only after having received forced medication. A few had suffered minor abrasions and two reported revived memories of prior abuse. Several believed that the use of restraint protected them from hurting themselves or others. Some believed the episode had damaged the provider-patient alliance. Patients that had psychotic symptoms during restraint were more understanding of staff’s decision to restrain.

Conclusions: It is important to debrief patients after restraint, thus helping patients understand why restraint was used and identify early problems that may arise following the intervention. It is necessary to train staff in the early detection of aggression and in the use of less restrictive interventions.

References:

NR180  Monday, May 3, 3:00 p.m.–5:00 p.m.
Psychiatric Inpatients’ Experiences With Restraint

Rolf Wynn, M.D., Spesialpsyk, UNN-Asgard, Tromsøe N-9291, Norway

Educational Objectives:
At the conclusion of this session, the participant should understand how the use of restraint may affect patients.

Summary:
Objective: To examine patients’ experiences with physical restraint.

Method: Twelve purposively sampled psychiatric inpatients at a Norwegian institution were interviewed after physical restraint. The data were analyzed with the method of Grounded Theory.

Results: Seven had concomitantly received forced medication. None had been debriefed. Patients gave refusal of medication, refusal to follow staff directions, or their own aggression, as reasons why they had been restrained. Most thought that restraint had been unnecessary. Being restrained evoked feelings of anxiety, anger, and hostility. Some calmed down in restraints only after having received forced medication. A few had suffered minor abrasions and two reported revived memories of prior abuse. Several believed that the use of restraint protected them from hurting themselves or others. Some believed the episode had damaged the provider-patient alliance. Patients that had psychotic symptoms during restraint were more understanding of staff’s decision to restrain.

Conclusions: It is important to debrief patients after restraint, thus helping patients understand why restraint was used and identify early problems that may arise following the intervention. It is necessary to train staff in the early detection of aggression and in the use of less restrictive interventions.

References:

NR181  Monday, May 3, 3:00 p.m.–5:00 p.m.
Neurocognitive Effect on Minor Sleep Deprivation

Wanseok Seo, M.D., Psychiatry Department, Yeunam University Hospital, Daemyung Dong Nambu, Daegu 705-717, South Korea; Jinsung Kim, M.D., Seungdeuk Cheung, M.D., Shinho Song, M.D., Eunjung Jung, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize that many minor sleep deprivation-related accidents are associated with visual, verbal function impairment.

Summary:
Sleep deprivation is one of the most common health problems and is associated with traffic accidents, disasters, and other accidents. We defined one night sleep deprivation as minor sleep deprivation and observed cognitive function differences between a normal sleep and minor sleep deprivation group. Healthy, non-caffeine addicted medical students recruited and randomly divided into normal sleep and minor sleep deprivation (mSD) groups. Initial test of Korean Forms of WAIS, memory assessment scales (MAS), continuous performance tests (visual, auditory), controlled CPT (visual, auditory) and WCST (Wisconsin Card Sorting Tests) were performed in the same situation. One week later, same tests were performed in different situation. Normal sleep people performed in the same situation. On the other hand sleep-deprived people stayed up all night in psychiatric ward with nighttime nurses, and repeated same tests. The results analyzed by Mann-Whitney U test, repeat measures ANOVA. Calculation in WAIS, verbal memory in MAS scores decreased in mSD group so, verbal ability was influenced by minor sleep deprivation. In visual CPT decreased correction numbers, increased commission errors observed in visual CPT. Finally, increased reaction times in all forms of CPT, CCPT were consistently observed. Even minor sleep deprivation causes verbal, visual function impairment, reaction time abnormality, and we conclude that many minor sleep deprivation-related accidents associated with visual, verbal function impairment.

References:
NR182  Monday, May 3, 3:00 p.m.-5:00 p.m.
The Phenomenology of Dual-Diagnosis Bipolar Disorder
Omar Elhaj, M.D., Psychiatry Department, Case Western School of Medicine, 11400 Euclid Avenue, Suite 200, Cleveland, OH 44106; Melvin D. Shelton III, M.D., Daniel J. Rapport, M.D., Eric A. Youngstrom, Ph.D., Kelly S. Sak-Jackson, M.A., Robert L. Findling, M.D., Joseph R. Calabrese, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the phenomenology of dual diagnosis bipolar disorder.

Summary:

Methods: Patients enrolled into ongoing clinical trials meeting DSM-IV criteria for rapid cycling and abuse/dependence on a substance(s) received research assessments.

Results: Of 165 dual-diagnosis bipolar patients, 78% were abusing/dependent on alcohol, 45% cannabis, 31% cocaine, and 4% other; 46% were using two or more substances and 15% were using three or more. Cannabis was abused in over half (54%) while alcohol and cocaine use led to dependence in nearly three quarters (77%, 71%) of the sample. Overall, 74% were bipolar I, 62% male, 52% were comorbid with an anxiety disorder, 40% privately insured, and 57% no insurance/Medicaid. Of those enrolled, 68% had been charged with legal offenses (39% were convicted of a serious offense and 34% incarcerated for a mean of 14 months), 46% had been previously diagnosed with bipolar disorder, 20% were never diagnosed with a mood disorder, and 33% had been incorrectly diagnosed with recurrent major depression. Mean delay from symptom onset to treatment was 18 years. The rate of legal complications in those who had never been publicly insured was 87%.

Conclusion: Patients with dual-diagnosis bipolar disorder are highly comorbid, complex, and poorly understood.

Funding Source(s): GlaxoSmithKline

References:
1. Regier, D; Farmer, M; Rae, D; et al: Comorbidity of mental disorders with alcohol and other drug abuse. JAMA 1990; 264:2511-2518.

NR184  Monday, May 3, 3:00 p.m.-05:00 p.m.
The Challenge of Healing: Identifying At-Risk Youth in Emergency Visits in France
Leon-Patrice Celestin, M.D., Pedopsy 78102, Chipoissy-Paris-West, 26 Rue de la Folie Regnault #26, Paris 75011, France; Smadar Westreich, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to: (1) Identify apparent complaints for use of emergency department; (2) Recognize underlying motives, links with age, psychosocial, risk-taking factors; and (3) Gain insight in clinical practice challenges for identifying youth who are at-risk for behavioural/emotional problems.

Summary:

Aim: To investigate French adolescents' motives for using the emergency department (ED) within the context of identifying at-risk youth.

Method: Retrospective survey of emergency department (ED) use during 12 weeks in a general hospital serving a large western-Paris suburban department, by adolescents (broad-defined age range 11-25).

Results: Adolescents' ED use accounted for 41% (N=3663; mean age=18, sd=4) of all youth visits (n=8956, ages 0-25, mean=9.3; sd=7.9), consisting of early (EA, ages 11-14, 27%), middle (MA, ages 15-17, 20%), late adolescents (LA, ages 18-21, 27%) and adolescents (AU, ages 21-25, 25%). Most visits resulted in
discharge without psychiatric/psychological referral (86.8%). Main consultation motives were injury-related trauma (33.2%) including more violent incidents in difficult sociodemographic subregions, non-specific complaints (27.7%), digestive complaints (18.1%), specific non-accidental somatic motives (17.6%). Adolescents were more likely involved in injury-related visits compared with younger children (57.3% vs 42.7%, P<0.0001), explicit psychiatric/psychosocial motives (3.4%) concerned more late adolescents (37.4% vs 13% EA, 24.4% MA, 25.2% AU).

Conclusion & implications: Findings convey need for systematizing emergency consultations’ screening for adolescents’ risk taking, and behavioral and emotional problems through implementation of standardised protocols. Practitioners’ education about psychological components of somatic consultation motives will be instrumental herein. Sociodemographic factors should be addressed through specific adolescent service development.

References:

NR185 Monday, May 3, 2004, 3:00 p.m.-5:00 p.m.
Venlafaxine Extended Release as a Treatment for GAD in Children and Adolescents
Supported by Wyeth Pharmaceuticals
Moira A. Rynn, M.D., Department of Psychiatry, University of Pennsylvania, 3535 Market Street, Suite 670, Philadelphia, PA 19104-3309; Paul P. Yeung, M.D., Mark A. Riddle, M.D., Nadia R. Kunz, Pharm.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to review the efficacy and safety data regarding venlafaxine ER in the treatment of children and adolescents with generalized anxiety disorder.

Summary:
Background: Venlafaxine ER is an effective treatment for adults with (GAD): no data are available in pediatric patients.

Methods: Results were combined from two, 8-week, multicenter, placebo-controlled, double-blind, flexible-dose studies in 175 children (aged 6–11 years) and 145 adolescents (aged 12–17 years) randomly assigned to receive venlafaxine ER (dose by weight; n=157) or placebo (n=163). The primary efficacy variable was the Columbia KIDDIE-SADS GAD total score for 9 delineated items; primary endpoint was the final on-therapy evaluation. Secondary efficacy variables were total scores on the C-KIDDIE-SADS GAD (also individual Severity and Impairment scores), PARS, HAM-A, SCARED Parent and Child Forms, and CGI-S and CGI-I scales.

Results: Venlafaxine-treated patients had an adjusted mean decrease of 17.4 points on the primary efficacy variable versus 12.7 for the placebo group (P<0.001). Secondary measure results were similar. Response (CGI-I score <3) rates were 69% and 48% for the venlafaxine and placebo groups, respectively (P<0.001). The most common ≥25% and ≥2x placebo adverse events were asthenia, anorexia, pain, and somnolence. There were no suicides in these studies.

Conclusion: Venlafaxine ER may be an effective treatment in children and adolescents with GAD. Prescribers should be alert to signs of suicidal ideation in pediatric patients taking venlafaxine.

References:

NR186 Monday, May 3, 2004, 3:00 p.m.-5:00 p.m.
Are There Reliable Neuropsychological Deficits in OCD?
H. Blair Simpson, M.D., Department of Psychiatry, Columbia University, 1051 Riverside Drive Unit 69, New York, NY 10032; Jonathan Huppert, Ph.D., Wilma Rosen, Ph.D., Shu Hsing Lin, Ph.D., Edna B. Foa, Ph.D., Michael Liebowitz, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to evaluate whether there are reliable neuropsychological deficits in OCD.

Summary:
Background: This study’s aim was to replicate prior findings that subjects with obsessive-compulsive disorder (OCD) have deficits in executive functioning, nonverbal memory, and/or motor speed and then to determine whether these deficits impact functioning.

Methods: Sixty-five adults with OCD and 35 matched healthy controls participated in an evaluation of their clinical state and performance on various neuropsychological tasks, including tasks that assess executive functioning, nonverbal memory, and motor speed. Primary analyses compared subjects with current OCD (n=30) and healthy controls (n=35). Secondary analyses examined the effects of comorbidity and prior OCD history.

Results: Subjects with current OCD differed significantly from controls only on the Benton Visual Retention Test (BVRT) and the Block Design subtest from the Wechsler Abbreviated Scale of Intelligence. Only BVRT performance distinguished healthy controls (n=35), subjects with current OCD (n=30), subjects with current OCD and comorbidity (n=15), and subjects with a history of OCD (n=16). OCD severity had no significant effect on neuropsychological performance.

Conclusions: We found few differences between OCD subjects and healthy controls in neuropsychological performance, challenging the specificity of previously identified deficits in executive functioning, nonverbal memory, and motor speed for OCD. Whether neuropsychological deficits contribute to functional impairment in OCD requires further study.

Funding Source(s): MH45436-0651, MH45404-0651

References:

NR187 Monday, May 3, 2004, 3:00 p.m.-5:00 p.m.
Pre-Traumatic Factors That Predict Post-Traumatic Stress Symptoms
Sharon Gil, Ph.D., Department of Nursing, University of Haifa, Mount Carmel, Haifa 31905, Israel
Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the role played by pre-traumatic factors in the development of post-traumatic stress symptoms (PTSS).

Summary:

Objectives: The focus of the present study is to examine the role played by pre-traumatic factors in the development of post-traumatic stress symptoms (PTSS) among a healthy population exposed to a terrorist attack.

Method: Participants were 180 undergraduate students who were initially evaluated two weeks prior to a terrorist explosion on a bus near the University of Haifa, Israel. They were then re-evaluated at one week and at one month after the explosion. Assessment included a personality questionnaire (the Tridimensional Personality Questionnaire—TPQ); a coping style questionnaire (the Multidimensional Coping Inventory—COPE); and an estimation of PTSS, using the PTSD Symptom Scale—Self Report (PSS).

Results: Stepwise regression analysis revealed four variables predicting PTSS levels at one week: history of traumatic exposure; low problem-focused coping style; high avoidance coping style; and high harm avoidance tendencies. At one month, four variables appeared to predict PTSS levels: history of traumatic exposure, low emotional-focused coping style, high avoidance coping style, and high harm avoidance tendencies.

Conclusions: Pre-traumatic factors are closely related to the risk of developing PTSS and can thus be utilized for preventive identification and early intervention among those who are at such risk.

References:


NR188 Monday, May 3, 3:00 p.m.-5:00 p.m.

Prolactin Response to d-Fenfluramine in Combat-Related PTSD

Isaac Schweitzer, M.D., Psychiatry Department, Melbourne University, 130 Church Street, Richmond, Melbourne VIC 3121, Australia; Philip Morris, Ph.D., Malcolm Hopwood, M.D., Kay Maguire, Ph.D., Trevor Norman, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should better understand serotonergic function in PTSD.

Summary:

Introduction: Central serotonergic function can be investigated by measuring the prolactin response to the serotonin releasing/uptake agent, d-fenfluramine. This study investigated the effect of diagnosis, depressive symptoms and history of alcohol or tobacco abuse or dependence on the d-fenfluramine test in combat-related post-traumatic stress disorder (PTSD).

Method: Male, non-hospitalized combat-exposed veterans diagnosed with PTSD (DSM-IV-R) and a similarly aged combat-exposed control group were assessed for both PTSD and depressive symptoms and prolactin responses to a 30mg d-fenfluramine challenge test. Ninety-five subjects were studied; 23 were controls, 46 subjects met the criteria for current PTSD, and 26 for past PTSD.

Results: There were no significant differences between the three groups for baseline prolactin, peak prolactin, and time to reach peak, delta prolactin, or area under the curve of the prolactin v. time curve. Depressive symptoms and history of alcohol or tobacco abuse or dependence did not have a confounding effect on the prolactin responses to d-fenfluramine.

Conclusions: This study suggests that a blunted prolactin response to d-fenfluramine may be a consequence of combat exposure rather than PTSD. To confirm this, further studies involving both healthy and combat-exposed control groups in addition to subjects with PTSD of similar ages are required.

References:


NR189 Monday, May 3, 3:00 p.m.-5:00 p.m.

Increases in ACTH Suppression After DST in Adolescents With PTSD

Fabrice Duval, M.D., Department of Psychiatry, Centre Hospitaller, 27 Rue du 4eme RSM, Ruffach 68250, France; Marc-Antoine Crocq, M.D., Marie S. Guillon, M.D., Marie Claude Mokrani, Ph.D., Jose Monreal, M.D., Jean-Paul Macher, M.D.

Educational Objectives:

At the end of this presentation, the participant should be able to understand that hypothalamic-pituitary-adrenal axis abnormality of PTSD (i.e. upregulation of glucocorticoid receptors) is already present in adolescents despite the short period elapsed since trauma.

Summary:

Background: Evidence suggests that individuals with posttraumatic stress disorder (PTSD) have an enhanced sensitization of the hypothalamic-pituitary-adrenocortical (HPA) axis. However, few studies in adolescents have been performed.

Method: Fourteen sexually-abused adolescent inpatients with DSM-IV PTSD were compared with 14 adolescent hospitalized controls. All subjects underwent a standard dexamethasone suppression test (DST, 1 mg given orally at 11 PM) five days after admission. Baseline blood samples were obtained at 8 AM, and the following day, adrenocorticotropin (ACTH) and cortisol levels were measured at 8 AM, 4 PM, and 11 PM. Clinical assessment included the impact of Event Scale, Stanford Acute Stress Reaction Questionnaire, Beck Depression Inventory, and Coping Inventory for Stressful Situations.

Results: Post-DST ACTH levels were significantly lower in PTSD than in control adolescents (at 8 AM: p<0.005; at 4 PM: p<0.001; at 11 PM: p<0.05). In patients, post-DST cortisol levels were reduced but not significantly. No correlations were found between ACTH and cortisol levels and the scale and questionnaire scores, nor with time elapsed since trauma.

Conclusion: These results demonstrate that sexually-abused adolescents with PTSD show ACTH hypersuppression to DST suggesting enhanced glucocorticoid receptor sensitivity in the pituitary.

References:

NR190  Monday, May 3, 3:00 p.m.-5:00 p.m.
Quality-of-Life Assessment in Anxiety Disorders: A Psychometric Evaluation

Nicholas Maltby, Ph.D., Anxiety Disorders Center, Institute of Living, 200 Retreat Avenue, Hartford, CT 06106; Gretchen Diefenbach, Ph.D., David Tolin, Ph.D., Johanna Crocetto, M.S., Patrick Worhunsky, B.S.

Educational Objectives:

At the conclusion of this session, the participant should be able to make informed choices when selecting measures to assess the impact of anxiety disorders on quality of life.

Summary:

Objectives: The negative impact of anxiety disorders on quality of life has increasingly been noted. As a result, there has been increased emphasis on evaluating quality of life when assessing treatment outcome. The objective of the present study was to examine the psychometric properties of three commonly used quality of life measures among a group of patients with anxiety disorders.

Methods: Sixty-four patients presenting for treatment at an outpatient anxiety disorders clinic completed the Quality of Life Inventory (QOLI), the Social Adjustment Scale (SAS), and the Sheehan Disability Scale (SDS). Diagnostic status was determined using the Anxiety Disorders Interview Schedule for DSM-IV. Overall severity of illness was rated using clinical global impressions ratings.

Results: All three measures possess adequate convergent and discriminant validity. However, in a discriminant function analysis, only the SDS family life/home responsibilities scale and the QOLI entered the equation. Together, they correctly classified 100% of non-anxious participants and 90% of anxiety disordered patients.

Conclusion: While all measures possess adequate reliability and convergent and discriminant validity when assessing patients with anxiety disorders, the SDS family life/home responsibilities scale and the QOLI were superior in discriminating between patients with anxiety disorders and non-anxious controls.

References:


NR191  Monday, May 3, 3:00 p.m.-5:00 p.m.
Tryptophan Hydroxylase is Linked Among Korean Patients With Panic Disorder

Hun Gu Park, M.D., Seoul Paik Hospital, 85 Jurdong-2-Ga, Chung-Gu, Seoul 100-032, Korea; Young-Hee Choi, M.D., Jong-Min Woo, M.D., Dae Yeon Cho, Kyung Sik Yoon, M.D., Hun Gu Park, M.D., Woo Yeon Cho, M.A., Haye Young Yoon, M.A.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the possibility of the association between tryptophan hydroxylase and panic disorder.

Summary:

Objective: Tryptophan hydroxylase (TPH) is the late limiting enzyme in the synthesis of serotonin. We assessed whether the allelic constitution of the TPH gene is associated with panic disorder.

Method: One hundred and fifty-five patients with panic disorder and 102 normal healthy comparison subjects were tested for a genetic polymorphism of TPH A218C, serotonin transporter linked polymorphic lesion, catechol-O-methyltransferase G472A, C408G, cytochrome P450 2D6(CYP2D6), CYP2C19*2, CYP2C19*3.

Results: The frequency of cc genotype of TPH was significantly lower in the patients with panic disorder than in the healthy subjects (16.36% vs 30.77%, x^2=6.339, p=0.042, df=2). Genotypes of other genes of panic disorder did not significantly different from the control group.

Conclusions: These results suggest that the genotype of the TPH gene polymorphism may be related to the panic disorder.

References:


NR192  Monday, May 3, 3:00 p.m.-5:00 p.m.
5-HTTLPR and COMT Gene Polymorphisms Among Korean Panic Patients

Young-Hee Choi, M.D., Seoul Paik Hospital, 85 Jurdong-2-Ga, Chung-Gu, Seoul 100-032, South Korea; Jong-Min Woo, M.D., Dae Yeon Cho, Kyung Sik Yoon, M.D., Hun Gu Park, M.D., Woo Yeon Cho, M.A., Haye Young Yoon, M.A.

Educational Objectives:

At the conclusion of this session, the participant should understand that 5-HTTLPR and COMT polymorphisms relate to the treatment outcome of panic disorder with paroxetine.

Summary:

Objective: Genetic variation of the promoter for the serotonin transporter linked polymorphic region (5-HTTLPR) gene and catechol-O-methyltransferase (COMT) gene has been associated with its functional capacity. The authors tried to find the relationship between these genes and the treatment outcome of panic disorder with paroxetine.

Method: One hundred and seven patients with panic disorder entered this study and 78 patients were completed. The patients were treated with paroxetine 10–20mg for ten weeks. The severity of panic disorder was assessed with Clinical Global Impression (CGI) scale and Panic Disorder Severity Scale at the first visit, first week, second week, sixth week, and tenth week.

Results: 5-HTTLPR is and II variants were associated with better response in CGI when compared with ss variants at two weeks of paroxetine treatment (t=2.57, p=0.013). COMT C408G gg variants were associated with better response in CGI at six weeks of treatment (F=3.72, p=0.031). There was no linkage between 5-HTTLPR and COMT gene polymorphisms and panic disorder.

Conclusions: This result shows that the 5-HTTLPR and COMT gene polymorphisms may be related to the treatment outcome of panic disorder with paroxetine.

References:

NR193  Monday, May 3, 3:00 p.m.-5:00 p.m.
Evaluating a New Anxiety Screening, Severity, and Outcome Measure: “What If?”
Margaret D. Weiss, M.D., Psychiatry Department, UBC, B430-4500 Oak Street, Vancouver, BC V6H 3N1, Canada; Kenneth D. Gadow, Ph.D., Michael B. Wasdell, M.A., Joyce Sprafkin, Ph.D., Melissa M. Bomben, M.S.C.
Educational Objectives:
At the conclusion of this session, the participant should be able to describe the psychometric properties of the WHAT IF and indicate how the WHAT IF could facilitate diagnostic evaluations.
Summary:
Objective: The WHAT IF rating scale is a simple, self-report measure of worry and anxiety, designed to screen for anxiety in all ages. Existing measures of anxiety place a heavy emphasis on somatic symptoms, which do not discriminate anxiety disorders well. The WHAT IF screens for DSM-IV diagnostic criteria and breadth and depth of symptoms. Validity and reliability of the WHAT IF in an adult sample were evaluated.
Method: 352 participants, aged 18–41 years, completed the WHAT IF and the Adult Self-Report Inventory 4 (ASRI-4), which is a norm-referenced rating scale of DSM-IV psychiatric symptoms. A sub-sample (N=217) contributed to re-test reliability data.
Results: Internal consistency was high for subscales measuring diagnostic criteria, breadth of anxiety, and depth of anxiety (Cronbach’s alphas 0.94, 0.89 and 0.92, respectively). Test-retest correlations were good (diagnosis 0.85, breadth 0.79, depth 0.78, total score 0.86). Convergent validity of the WHAT IF total score was highest with ASRI-4 generalized anxiety disorder subscale (correlation coefficient 0.73). Discriminant validity between the WHAT IF and ASRI-4 was consistent with anticipated outcomes.
Conclusions: This study found the WHAT IF to be a reliable and valid clinical measure of anxiety in adults.
References:

NR194  Monday, May 3, 3:00 p.m.–5:00 p.m.
Venlafaxine Extended Release Versus Placebo in the Short-Term Treatment of Panic Disorders
Supported by Wyeth Pharmaceuticals
Michael R. Liebowitz, M.D., Anxiety Disorder, New York State Psychiatric Institute, 1051 Riverside Drive, Unit 120, New York, NY 10032-2603; Gregory M. Asnis, M.D., Evan Tzanzis, Timothy M. Whitaker, M.D.
Educational Objectives:
At the conclusion of this session, the participant should be able to evaluate the efficacy, safety and tolerability of venlafaxine XR in the treatment of panic disorder, relative to placebo, and understand the importance of measuring multiple domains in assessing treatment effectiveness for panic disorder.
Summary:
Objective: To evaluate the efficacy, safety, and tolerability of venlafaxine XR in short-term treatment of panic disorder.
Methods: In this multicenter, double-blind study, 345 adult outpatients with DSM-IV panic disorder (≥ agoraphobia) were randomized to flexible-dose venlafaxine XR (75–225 mg/day) or placebo for ten weeks (n=155 per group, ITT population). The primary outcome measure was the percentage of panic-free patients (PAAS). Key secondary measures included PDSS score and CGI-I response (score=1 or 2).
Results: At endpoint (final on-therapy evaluation), there was a trend (P = 0.056) toward a greater percentage of panic-free patients in the venlafaxine XR group (51%) vs placebo (41%). When adjusted for baseline severity, reduction in PAAS full-symptom panic attacks was significantly (P=0.040) greater for venlafaxine XR vs placebo. Mean change from baseline in PDSS total score was significantly (P=0.020) greater for the venlafaxine XR group (8.90) vs placebo (7.36), and significantly (P=0.031) more venlafaxine XR-treated patients achieved CGI-I response (71%) vs placebo (59%) at the final on-therapy evaluation. Treatment with venlafaxine XR was generally safe and well tolerated. Discontinuation due to adverse events was low in both groups (6% venlafaxine vs 5% placebo).
Conclusion: Venlafaxine XR was effective, safe, and well-tolerated in short-term treatment of panic disorder.
Funding Source: Wyeth Research
References:

NR195  Monday, May 3, 3:00 p.m.–5:00 p.m.
Adjunctive Topiramate in Treatment-Resistant OCD
Michael A. Van Ameringen, M.D., Department of Psychiatry, McMaster University, 1200 Main Street, West, Hamilton, ON L8N 3S5, Canada; Catherine L. Mancini, M.D., Beth Pipe, B.S.C., Mark Bennett, B.A.
Educational Objectives:
At the conclusion of this session, the participant should be able to: (1) understand the potential benefit of adding the topiramate in treatment-resistant OCD; and (2) examine the potential role of glutamate involvement in the neurobiology of OCD.
Summary:
Background: Serotonin reuptake inhibitors (SRIs) are considered first-line treatments for obsessive-compulsive disorder (OCD), with response rates ranging from 42% to 53%. Many patients achieve some response but remain symptomatic despite an adequate SRI trial. Recent neuroimaging data found abnormally high glutamatergic concentrations in children with OCD. Following SRI treatment, a decrease in OCD symptom severity was associated with a decrease in caudate glutamatergic concentrations. We initiated an investigation of adjunctive topiramate (an anticonvulsant agent with glutamatergic properties) in the treatment of non-remitted OCD patients.
Method: Sixteen consecutive OCD outpatients, who were partial or nonresponders to SRI monotherapy or SRI combination therapy (antipsychotic, other antidepressant, or benzodiazepines) had topiramate added over nine to 26 weeks. Baseline and endpoint Clinical Global Impression-Severity (CGI-S) and CGI-Improvement (CGI-I) were evaluated.
Results: Ten of 16 patients were responders (62.5%) with a CGI-I score of much or very much improved. The mean dose of topiramate was 253.1 ± 93.9 mg/day. The mean time to response was 9.0 ± 4.3 weeks. CGI-S scores decreased significantly from baseline to endpoint, from 6.1 ± 0.9 to 4.5 ± 1.3 (p <.001).

Discussion: This case series suggests some preliminary evidence that the addition of topiramate may be useful in treatment-resistant OCD. This study may add further support to the presence of glutamatergic abnormalities in some OCD patients.

References:

NR196  Monday, May 3, 3:00 p.m.–5:00 p.m.
An Open Trial of Topiramate Treatment of Generalized Social Phobia
Supported by Janssen-Ortho, Inc.
Michael A. Van Ameringen, M.D., Department of Psychiatry, McMaster University, 1200 Main Street, West, Hamilton, ON L8N 3Z5, Canada; Catherine L. Mancini, M.D., Beth Pipe, B.S.C., Mark Bennett, B.A., Jonathan Oakman, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to understand the potential use of topiramate in the treatment of generalized social phobia.

Summary:
Objective: Selective serotonin reuptake inhibitors (SSRIs) are the current gold standard in the pharmacological treatment of generalized social phobia (GSP). Unfortunately, these treatments are only effective in approximately 50% of individuals with GSP, and are associated with significant side effects. Based on the successful use of the anticonvulsants, in treating GSP, we conducted an open trial of the anticonvulsant topiramate (TPM) in GSP.
Method: Seventeen adult outpatients with GSP were entered into a 16-week, open trial of TPM. Primary efficacy measures were the number of responders with a Clinical Global Impression-Improvement Scale (CGI-I) score of 1 or 2 (very or much improved) at week 16, and the change from baseline to end point in the Liebowitz Social Anxiety Scale (LSAS).
Results: Eleven of 17 patients completed the trial. Of the completers 8/11 (72.7%) were responders at 16 weeks with a mean drop in LSAS score of 46.5%. In the intent to treat (ITT) analysis 9/17 (52.9%) were responders by CGI-I. The mean drop is LSAS score for the ITT group was 32.1%. The change in LSAS from baseline to endpoint was also significant for the ITT group, (F= 4.252, df=4, p=.004).
Conclusion: Topiramate may be effective in the treatment of GSP and suggests that the neurobiology of GSP may involve both Glutamate and GABA systems.

Funding Source(s): Partially Funded by Janssen Ortho

References:

NR197  Monday, May 3, 3:00 p.m.–5:00 p.m.
Mood and Anxiety Disorder Referral Rates for Adults Attending a City Health Fair
Supported by Pfizer Inc.
Renee Rivera, M.S.W., Director of Community Services, Mental Health Association of Colorado, 6795 E. Tennessee Avenue, Suite 425, Denver, CO 80222; Timothy Hartman, Pharm.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to: (1) recognize the prevalence of concomitant mood and anxiety disorders in a health fair population; and (2) identify trends in referrals from year to year and provide appropriate education information.

Summary:
Methods: The Mini International Neuropsychiatric Inventory(TM) tool was administered by mental health care professionals to 500 adults in 2002 and 501 adults in 2003. Effects of gender, year of screening, and ethnicity were examined using SPSS v 11.0.
Results: There were no differences between average ages. Ethnicity by year 2002 vs. 2003: Caucasian 93% vs. 92%; Hispanic 8.2% vs. 11.4%; African American 4.2% vs. 4%. Patients who were referred for mood or anxiety disorder follow-up increased significantly (p<0.001) from 2002 (227) to 2003 (276). The only gender significant differences in 2002 (p<0.001) and 2003 (p= 0.041) occurred in referrals for panic. Women outnumbered men (110 vs. 42 in 2002; 55 vs. 18 in 2003). While the number of referrals increased from 2002 to 2003 for OCD, PTSD, GAD, and social anxiety, only panic disorder increased significantly (p= 0.005). Combination disorders were found in greater than 60% of the time in 2002 except for depression at 40%. In 2003, the combination of disorders were greater than 70%. There were significant increases in the number of people with combination disorder between 2002 and 2003 for those with depression (p<0.001) and OCD (p=0.036).
Conclusion: The use of repeated screening instrument for mood and anxiety disorders may yield important prevalence information, which allows more precise interventions and funding for adults in the state.

Funding Source(s): Pfizer/Mental Health Association

References:

NR198  Monday, May 3, 3:00 p.m.–5:00 p.m.
Risperidone Treatment of PTSD Related to Childhood Abuse
Supported by Janssen Pharmaceutica and Research Foundation
D. Bradford Reich, M.D., Department of Psychiatry, McLean Hospital, 115 Mill Street, Belmont, MA 02478; Sherry Winternitz, M.D., John Hennen, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize the symptoms of posttraumatic stress disorder
related to childhood abuse in women and to understand the role of risperidone in treating them.

Summary:

Background: This study evaluated the effectiveness of risperidone in the treatment of posttraumatic stress disorder (PTSD) related to childhood physical, sexual, verbal, and emotional abuse in women.

Method: Subjects were outpatient adult women, age 18–65, with chronic PTSD related to childhood physical, sexual, verbal, or emotional abuse. Subjects met DSM-III-R criteria for PTSD and criteria for PTSD on the clinician-administered PTSD Scale, one-month version (CAPS-1). Subjects were randomly assigned to receive flexible-dose risperidone (N=11) or placebo (N=9) for eight weeks. The primary outcome measure was change from baseline on the Clinician-Administered PTSD Scale, one-week version (CAPS-2). Secondary outcome measures were changes from baseline on the Impact of Events Scale (IOES), the Hamilton Depression Scale (HAM-D), the Hamilton Anxiety Scale (HAM-A), the Symptom Checklist-90 Revised (SCL 90-R), and the Dissociative Experiences Scale (DES).

Results: Risperidone-treated patients had significantly greater reductions in the CAPS-2 total score, intrusive and hyperarousal subscales of the CAPS-2, HAM-D, HAM-A, DES, and SCL-90. Conclusion: This study indicates that risperidone is a safe and effective treatment for intrusive and hyperarousal symptoms in adult women with chronic PTSD from childhood physical, sexual, verbal, and emotional abuse.

Funding Source(s): Janssen Pharmaceutical

References:

NR199 Monday, May 3, 3:00 p.m.-5:00 p.m. Assessing Onset of Symptom Relief in Patients With GAD Supported by Pfizer Inc.

Robert J. Morlock, Ph.D., Department of Outcomes, Pfizer Inc., 2800 Plymouth Road, Ann Arbor, Ml 48105; Douglas E. Feltner, M.D., Sheri Feinheil, Ph.D., Valerie Williams, Ph.D., Joseph Capponi, Ph.D., Janet Harness, M.D., Richard J. Kavoussi, M.D., Jean Endicott, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should understand the order of symptom improvement as described by patients and clinicians.

Summary:

Background: Fast acting anxiety medications are important to patients and society. Measuring early onset, however, requires a sensitive and clinically responsive measure.

Objectives: To develop an instrument to assess onset of symptom relief within the first week of treatment.

Methods: To identify relevant constructs of interest, a series of clinician interviews and patient focus groups were conducted according to structured guides. Participants were first asked very general questions about their experiences with GAD and then discussions focused on early symptom improvement. Participants were asked which changes tend to occur first with treatment and which changes are most important from the patients’ perspective.

Cognitive interviews assessed the understandability of each construct.

Results: There was consistency across the focus groups and clinicians in the description of symptoms that improve first—the alleviation of anxiety, worries, tension, and irritability, as well as improved sleep and cognitive functioning (e.g., concentration, memory). These same symptoms were also rated by the majority of participants as very important and frequently included among the patients’ most bothersome symptoms.

Conclusions: This study identified an initial set of items developed specifically to measure onset of symptom relief in patients with GAD within the first week of treatment.

Funding Source(s): Pfizer

References:
NR201  Monday, May 3, 2004, 3:00 p.m.-5:00 p.m.
Social Phobia and Panic Disorder: Responses to the Carbon Dioxide Challenge Test
Marco A. Mezzasalma, M.D., Psychiatric Institute, University Fed Rio de Janeiro, Rua Caning 21701, Rio de Janeiro, RJ 22081-040, Brazil; Antonio E. Nardi, M.D., Alexandre M. Valenza, M.D., Fabiana L. Lopes, M.D., Isabella Nascimento, M.D., Rafael C. Freire, M.D., Walter A. Zin, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize that the CO2 challenge test may be a good laboratorial model for the study of social phobia.

Summary:
Objectives: Our aim was to compare the response of panic disorder (PD) patients with social phobia (SP) patients and patients with both diagnosis (comorbid) after a 35% CO2 challenge test.

Methods: We randomly selected 26 PD patients, five SP patients and six PD and SP patients (DSM-IV). These patients were drug free for at least one week and received two vital capacity inhalations of a carbogenic mixture (35% CO2 and 65% O2) and compressed atmospheric air (placebo) chosen randomly and separated by a 20-minute interval.

Results: A total of 69.2% (n=18) PD patients, 20% (n=1) SP patient and 33.3% (n=2) PD and SP patients had a panic attack after the CO2 inhalation. We also found that 61.5% (n=16) PD patients, 60% (n=3) SP patient and 50% (n=3) PD and SP patient had an increase in the Subjective Units of Disturbance Scale (SUDS) equal or greater than 3 after CO2 inhalation.

Discussion: The 35% CO2 inhalation challenge already is a useful tool for laboratorial investigation of panic disorder. Social phobia patients tend to respond similarly, so this test may prove to be a good laboratorial model for the study of social phobia.

References:

NR202  Monday, May 3, 2004, 3:00 p.m.-5:00 p.m.
The Associations Between Obsessive-Compulsive Cognitive Domains and OCD Symptom Subtypes
Neil A. Rector, Ph.D., Mood and Anxiety Clinic, Clarke Institute, 250 College Street, Toronto, ON M5T 1R8, Canada; Margaret A. Richter, M.D., Kate Szacun-Shimizu, B.A., Danielle Bourdeau, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to: (1) identify dimensional versus categorical models of symptom expression in OCD; (2) evaluate previous research on the relations between obsessive-compulsive beliefs and appraisals and different symptom subtypes in OCD; and (3) recognize the treatment implications for distinct cognitive-symptom subtypes in OCD.

Summary:
Introduction: There is growing interest in the possibility of distinct symptom subtypes in OCD. This study aimed to assess the relations among O-C beliefs and appraisals and the seminal symptom subtypes of OCD.

Method: Participants were 125 consecutive referrals meeting criteria for a primary DSM-IV (APA, 1994) diagnosis of OCD. All participants completed the Yale-Brown Obsessive Compulsive Scale (Y-BOCS; Goodman et al., 1989), the Obsessive Belief Questionnaire (OBQ-44; OCCWG, 2003) and the Interpretations of Intrusions Inventory (III; OCCWG, 2003).

Results: Exploratory factor analysis of the 15 rationally derived categories of obsessions and compulsions resulted in an interpretable four-factor solution: hoarding obsessions/compulsions, contamination obsessions/cleaning compulsions, symmetry/ordering, and obsessional (aggressive, religious, somatic)/checking. Examination of the cognitive predictors of the different symptom subtypes demonstrated that higher (OBQ) perfectionism/certainty scores uniquely predicted hoarding scores (t = 2.54, p < .01), higher (OBQ) importance/control scores uniquely predicted symmetry/ordering scores (t = 2.63, p < .01), higher (III) responsibility appraisal scores were uniquely predictive of pure obsession scores (t = 2.71, p < .005), and none of the cognitive factors predicted contamination scores.

Discussion: These results suggest that different O-C beliefs and appraisals are specifically associated with distinct O-C symptom clusters.

References:

NR203  Monday, May 3, 2004, 3:00 p.m.-5:00 p.m.
Cognitive and Behavioral Treatments for Medication-Refractory OCD
Neil A. Rector, Ph.D., Mood and Anxiety Clinic, Clarke Institute, 250 College Street, Toronto, ON M5T 1R8, Canada; Margaret A. Richter, M.D., Eileen Denisoff, Ph.D., Cynthia Crawford, M.S.C., Kate Szacun-Shimizu, B.A., Danielle Bourdeau, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to: (1) recognize the clinical approaches of exposure response prevention and cognitive therapy for OCD; (2) evaluate the empirical literature comparing the efficacy of ERP and CBT for OCD; and (3) be familiar with the current randomized control trial testing the additive benefits of ERP combined with CT for medication-refractory OCD.

Summary:
Introduction: A randomized, controlled trial was conducted to test whether a combined treatment intervention of Exposure/Response Prevention (ERP) plus cognitive therapy confers greater clinical gains than ERP alone for patients with medication-refractory OCD.

Method: Sixty-four participants meeting DSM-IV criteria for OCD were randomly assigned to receive either manual-based ERP+CT or ERP alone.

Measures: Yale-Brown Obsessive Compulsive Scale (Y-BOCS), The Obsessional Belief Questionnaire (OBQ-44), and The Interpretations of Intrusions Inventory (III), were administered at baseline and at post-treatment.

Results: Preliminary results demonstrate that both ERP+CT and ERP alone produce statistically significant change on blind ratings of obsessive-compulsive severity (Y-BOCS) from baseline (M = 23.65, SD = 4.57) to post-treatment (M = 14.84, SD = 7.12), F (1,35) = 105.20, p < .0005 (d = 1.47). A significant Treatment Group x Treatment Phase interaction, P (1,35) = 4.74, p < .05,
demonstrates that ERP+CT (Mean Pre-Post Y-BOCS Change = 10.5) leads to superior outcomes compared with ERP alone (Mean Pre-Post Y-BOCS Change = 6.8).

Discussion: These preliminary results provide support for the additive benefits of cognitive therapy strategies when delivered in combination with the well-validated behavioral approaches.

References:

NR204
Monday, May 3, 3:00 p.m.-5:00 p.m.
Obsessive Beliefs in the First-Degree Relatives of Patients With OCD

Neil A. Rector, Ph.D., Mood and Anxiety Clinic, Clarke Institute, 250 College Street, Toronto, ON M5T 1R8, Canada; Margaret A. Richter, M.D., Eliza Burroughs, B.A.

Educational Objectives:
At the conclusion of this session, the participant should be able to: (1) be familiar with the core cognitive beliefs that are hypothesized to contribute to the development of clinical obsessions; (2) to evaluate studies of vulnerability in non-affected first-degree relatives of patients with OCD; and (3) to recognize the significance of inflated responsibility as a core cognitive vulnerability for OCD.

Summary:

Introduction: This study investigated the frequency and breadth of obsessive beliefs hypothesized to be critical to the pathogenesis of obsessions in patients with OCD, their first-degree relatives, and in comparison to community norms.

Method and Measures: Twenty-two individuals comprising 11 probands meeting DSM-IV criteria for OCD and 11 non-affected first-degree relatives were assessed on a well-validated measure of obsessive beliefs tapping: (1) inflated responsibility/exaggerated threat estimation, (2) perfectionism/intolerance of uncertainty, and (3) overimportance of thoughts/controlling of thoughts (The Obsessive Belief Questionnaire; OBQ-44; Obsessive Compulsive Cognitions Working Group, 2003).

Results: Preliminary results demonstrate that patients with OCD have higher scores than their relatives on perfectionism/intolerance of uncertainty (t = 8.48, p < .009) and overimportance/control of thoughts (t = 4.59, p < .05), although scores on inflated responsibility/threat estimation were equivalent. There were no differences between relatives and controls on perfection/intolerance of uncertainty and overimportance/control of thoughts; however, relatives scored higher on inflated responsibility/threat estimation (t = 3.31, p < .01).

Discussion: While preliminary, these results support the prominence of inflated responsibility in OCD. If upheld in our larger sample currently being collected, inquiry into the putative genetic diathesis underlying cognitive vulnerability to OCD merits exploration.

References:
B.S.C., Eliza Burroughs, B.A., Nicole A. King, James L. Kennedy, M.D., Katharine A. Phillips, M.D.

Educational Objectives:

At the conclusion of this session, the participant should: (1) appreciate the contribution of genetic studies to improving understanding of the relationship between BDD and OCD; (2) recognize the significance and limitations of current knowledge regarding risk genes in psychiatric disorders.

Summary:

Introduction: Body dysmorphic disorder (BDD) is a relatively common and impairing disorder characterized by distressing and/ or impairing preoccupation with an imagined or slight defect in one's physical appearance. There is considerable evidence supporting a relationship between BDD and obsessive-compulsive disorder (OCD), an illness also associated with repetitive, intrusive and distressing thoughts, ideas, or impulses. In this study we set out to examine the genetic relationship between BDD and OCD, focussing on previously reported candidate genes.

Method: The promoter-region (5HTTLPR) (17q11.1-q12) polymorphism in the serotonin transporter gene and the gamma-aminobutyric GABA-γ2 gene (5q31.1-q33.2) were typed in 50 individuals with BDD (31 with primary BDD and 19 with OCD + co-morbid BDD) and 20 OCD subjects with subclinical BDD, and matched healthy controls of similar ethnicity and gender. Genotypes and allelic frequency were tested for all markers using chi-square analysis.

Results: BDD subjects showed association for GABA-γ2 (p=0.017), a trend for 5HTTLPR (P=0.064) was observed which became significant when comparing individuals with or without the dominant long allele (p=0.041). By contrast, only GABA-γ2 showed association in the subclinical BDD group (p=0.017).

Conclusions: This data suggests that there may be vulnerability genes unique to BDD as compared with subclinical BDD or OCD.

References:

NR207 Monday, May 3, 3:00 p.m.-5:00 p.m.

Speed of Onset of Benefit of Alprazolam Extended Release Versus Alprazolam-CT in Panic Disorder Supported by Pfizer Inc.

David V. Sheehan, M.D., Department of Psychiatry, University of South Florida, 3515 East Fletcher Avenue, Tampa, FL 33613-4706; Kathy H. Sheehan, Ph.D., B. Ashok Raj, M.D.

Educational Objectives:

At the conclusion of this session, the participant should understand how the speed of onset of clinical benefit of extended release alprazolam compares with the speed of onset of benefit of the original formulation in panic disorder.

Summary:

Introduction: Although the extended release (XR) formulation of alprazolam has been shown to be equivalent to regular alprazolam in terms of efficacy, and its duration of therapeutic benefit is known to be much longer, it is not known if alprazolam-XR has as fast an onset of clinical benefit as alprazolam-CT. A belief that it has a slower release has led some to consider it a maintenance and not a rescue treatment.

Methods: Structured diary records of hourly antianxiety benefit from a nine-week, open-label alprazolam-CT to alprazolam-XR switch study were used to examine the timing of onset and magnitude of clinical benefit on both formulations in 30 outpatients with panic disorder.

Results: The magnitude of benefit in the first hour after the first morning dose was similar before and after the switch to alprazolam-XR. The peak benefit and mean time to peak benefit were also similar and 90% of peak benefit was achieved in the first hour on both formulations.

Conclusion: The speed of onset of therapeutic benefit of extended release alprazolam is similar to that of the original formulation of alprazolam. The results suggest that extended release alprazolam may be used both as a rescue medication and as a maintenance treatment in panic disorder.

Funding Source(s): Research sponsored in part by Pfizer

References:

NR208 Monday, May 3, 3:00 p.m.-5:00 p.m.

Executive Dysfunction in the Panic Disorder: A New Finding?

Fabiana L. Lopes, M.D., Institute of Psychiatry, University FED Rio Jan, Min Octavio Kelly 467, AP1204-B, Niteroi, RJ 24220-300, Brazil; Antonio E. Nardi, M.D., Alexandre M. Valenca, M.D., Isabella Nascimento, M.D., Marco A. Mezzasalma, M.D., Walter A. Zin, M.D., Giampaolo Pema, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to determine if disexecutive syndrome is associated to panic disorder.

Summary:

Introduction: The prefrontal cortex might be involved in the neuropsychobiology of panic disorder. The aim of this study was to observe whether panic disorder is associated with a dysfunction of the prefrontal cortex, manifested by an executive dysfunction syndrome.

Method: A sample of 52 panic disorder (DSM IV) outpatients was compared with 43 healthy comparison subjects by means of the Brown Attention Deficit Disorder Scale and the DSM-IV criteria for current and past attention deficit hyperactivity disorder.

Results: Forty-two percent (n=22) of the patients with panic disorder had the “highly probable result” of an executive dysfunction (score 55 on the Brown Attention Deficit Disorder Scale compared with none (n=0) in the control group.

Conclusion: These results suggest that panic disorder may be associated with a disexecutive syndrome that might result from a prefrontal cortex dysfunction.

Funding Source(s): Brazilian Council for Scientific and Technological Development.

References:
2. Bystritsky A, Pontillo D, Powers M, Sabb FW, Craske MG, Bookheimer SY. Functional MRI changes during panic antici-
NR209  Monday, May 3, 2004, 3:00 p.m.-5:00 p.m.
Augmentation of SSRI Therapy for GAD With Tiagabine
Arifulla Khan, M.D., Psychiatry Department, Northwest Clinical Research Center, 1900 116th Avenue, N.E., Suite 112, Bellevue, WA 98004; Thomas L. Schwartz, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize the therapeutic potential of tiagabine as augmentation therapy in patients with GAD who remain symptomatic despite appropriate treatment with SSRIs.

Summary:
Objective: Preliminary findings suggest that tiagabine, a selective GABA reuptake inhibitor (SGRI), may reduce symptoms of anxiety and improve sleep. This study examined tiagabine as augmentation therapy to SSRIs in patients with GAD.

Methods: This eight-week, open-label study was designed to evaluate tiagabine in 50 patients with GAD who remained symptomatic despite appropriate SSRI treatment (<50% improvement of anxiety symptoms after ≥4 weeks at a stable, maximum recommended or tolerated dose). Tiagabine was initiated at 4 mg/d (2 mg bid) and then individually adjusted by 4 mg/w (2 mg bid/w) to a maximum of 16 mg/d (8 mg bid). Assessments included the HAM-A, Pittsburgh Sleep Quality Index (PSQI), and Sheehan Disability Scale (SDS).

Results: To date, 25 patients have at least one post-baseline, on-treatment assessment and are included in the analysis. Tiagabine further improved anxiety (HAM-A±SD baseline, 20.9±3.7; last observation, 11.7±8.1; P<0.001), with 40% of patients achieving remission (HAM-A<7). Tiagabine also improved sleep quality (PSQI: baseline, 10.0±3.7; last observation, 7.6±4.2; P<0.001) and patients’ overall functioning (SDS: baseline, 15.2±5.2; last observation, 10.5±6.7; P=0.001). Mean tiagabine dose was 10 mg/day (range: 4–16 mg/day). Most commonly reported adverse events were somnolence (n=6) and dizziness (n=4).

Conclusions: These preliminary findings suggest that tiagabine may be effective in patients with GAD who require augmentation of SSRI treatment.

References:

NR211  Monday, May 3, 2004, 3:00 p.m.-5:00 p.m.
A Phenomenological Comparison Between Hyperventilation and Spontaneous Panic Attacks
Isabella Nascimento, M.D., Department of Psychiatry, Federal University Rio Janeiro, Min Otavio Kelly 767 ap 1204-B, Niteroi, RJ 24220-300, Brazil; Antonio E. Nardi, M.D., Alexandre M. Valenca, M.D., Fabiana L. Lopes, M.D., Marco A. Mezzasalma, M.D., Walter A. Zin, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize that hyperventilation-induced panic attacks may be conformed as a sub-group of respiratory panic disorder subtype with its diagnostic implication.

Summary:
Objective: To assess symptoms of depression and anxiety in the largest cohort of fibromyalgia syndrome (FMS) patients yet evaluated.

Methods: 529 patients (91.5% female; mean age: 48.6; mean [SD] duration of FMS: 107.7 [100.5] months) diagnosed with FMS using ACR criteria completed a self-reported assessment, the Hospital Anxiety and Depression Scale (HADS), at the baseline visit in a randomized, monotherapy, controlled trial of pregabalin for FMS. Patients were excluded if they were taking TCAs or other antidepressants or sedatives.

Results: Baseline mean HADS scores [SD] fell in the mild range: 8.6 ± 4.0 for depression; 10.1 ± 4.3 for anxiety symptoms. 70% of patients scored in the normal (44%) or mild (26%) range, with 22% scoring in the moderate and 9% scoring in the severe categories for depressive symptoms. 55% of patients scored in the normal (29%) or mild (26%) category, with 28% scoring in the moderate and 17% scoring in the severe categories for anxiety symptoms. The percent of patients in the severe category for anxiety was greater than in the severe category for depressive symptoms.

Conclusions: Based on these results, anxiety disorders—and the potential impact of their symptoms—in patients with FMS deserves further study.

Study funded by Pizer.

References:
**Conclusion:** Our data suggest that there is an association between respiratory PD subtype and hyperreactivity to an acute hyperventilation challenge test. The HPA may be construed as a sub-group of respiratory PD subtype with diagnostic and therapeutic implications.

**References:**


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**NR212**

**Monday, May 3, 3:00 p.m.–5:00 p.m.**

**Respiratory and Automatic Panic Disorder Subtypes: Response to Alprazolam Extended Release Supported by Pfizer Inc.**

Karl Rickels, M.D., Department of Psychiatry, University of Pennsylvania, 3535 Market Street, Suite 670, Philadelphia, PA 19104-3309; Brian Klee, M.D., Charlotte Kremer, M.D.

**Educational Objectives:**

- This presentation should improve the participant’s understanding of the clinical presentation of panic disorder, and its safe and effective treatment with alprazolam-XR.

**Summary:**

**Background:** Research suggests that there are at least two clinically relevant subtypes of panic disorder (PD), a respiratory subtype and an autonomic subtype, each associated with different clinical characteristics. The current analysis evaluates the efficacy of alprazolam-XR (ALP-XR) in treating the respiratory and autonomic subtypes of PD.

**Methods:** Data were combined from 2 flexible-dose studies in which patients with PD were randomized, double-blind, to 6 weeks of ALP-XR (N=172; 59.9% female) or placebo (N=152; 59.3% female). A Sheehan Patient-Rated Anxiety Scale (SPRAS)-factor score > 8 was required to qualify a patient for either the respiratory or autonomic subtype (mod-to-severe on 4/5 symptoms).

**Results:** For the respiratory subtype (58% of total sample) ALP-XR resulted in greater improvement than placebo in total panic frequency at LOCF endpoint (-5.3 ± 0.65 vs. -2.9 ± 0.64; p = 0.01), and higher CGI-I responder rates (72% vs. 40%; p < 0.01). For the autonomic subgroup. ALP-XR resulted in similar superiority in reducing panic frequency (-5.3 ± 0.65 vs. -2.9 ± 0.64; p = 0.01), and achieving higher CGI-I responder rates (72% vs. 40%; p < 0.01). ALP-XR also significantly improved respiratory and autonomic symptomatology.

**Conclusion:** ALP-XR demonstrates significant efficacy in both the autonomic and respiratory subtypes of panic disorder.

**Funding Source(s):** Pfizer Inc.

**References:**


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**NR213**

**Monday, May 3, 3:00 p.m.–5:00 p.m.**

**Ocinaplon: A New Anxio-Selective Agent in Patients With GAD**

**Supported by Dov Pharmaceutical, Inc.**

Pal Czobor, Ph.D., Dov Pharmaceutical, Incorporated, 433 Hackensack Avenue, Hackensack, NJ 07601; Jill Stark, Phil Skolnick, Ph.D., Gary Beer, Arnold Lippa, Ph.D., Fred Duncanson, Bernard Beer

**Educational Objectives:**

- At the conclusion of this session, participants will obtain detailed information about the efficacy and safety profile of a potential new “anxioselective” agent that alleviates both psychic and somatic symptoms in GAD and offers a fast onset of action.

**Summary:**

**Background:** Despite the fact that patients with generalized anxiety disorder suffer from a wide range of disabling psychic and somatic symptoms, current drug therapies for GAD offer only limited relief across this range of symptoms. Preclinical experiments and phase II investigation suggest that ocinaplon, a novel non-sedating, non-benzodiazepine compound, possesses powerful anxiolytic effects and that these effects may encompass both psychic and somatic symptoms.

**Objective:** The goal of this study was to investigate whether ocinaplon can elicit improvement in both psychic and somatic symptoms.

**Methods:** The data for the purpose of the analyses were combined from two short-term, multicenter, double-blind, placebo-controlled trials of patients with the DSM-IV diagnosis of GAD (N = 187). The two studies had similar design, including a placebo run-in period during which initial assessments of patient eligibility, placebo response and compliance with treatment were evaluated.

**Results:** Ocinaplon produced statistically significant improvement in both psychic and somatic symptoms. A significant improvement was observed as early as after one week of dosing. The safety profile reveals no patterns of treatment-emergent events, including those effects normally associated with other anxiolytic and/or benzodiazepine compounds.

**Conclusion:** In contrast to SSRIs that reduce primarily psychic symptoms or benzodiazepines that act predominantly on somatic symptoms, ocinaplon produces improvement on a broad range of psychic and somatic symptoms. Overall, ocinaplon is a safe and effective treatment for GAD that offers a fast onset of anxiolytic action.

**Funding Source(s):** POV Pharmaceutical, Inc.

**References:**


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**NR214**

**Monday, May 3, 3:00 p.m.–5:00 p.m.**

**Double-Blind Comparison of Escitalopram and Paroxetine in the Long-Term Treatment of GAD Supported by Forest Laboratories, Inc.**

Robert J. Bielski, M.D., Health Department, Summit Research Net. Institute, 4084 Okemos Road, Suite A, Okemos, MI 48864-3258; Anjana Bose, Ph.D., Chung-Chi Chang, Ph.D.
At the conclusion of this session, the participant should be able to evaluate the relative efficacy and tolerability of escitalopram 10–20 mg/day compared with paroxetine 20–50 mg/day in the long-term treatment of generalized anxiety disorder.

Background: Escitalopram is the most selective SSRI studied to date, and has been shown in three randomized, placebo-controlled, double-blind trials to be effective and well tolerated in treating GAD. There are few studies, however, that compare the efficacy and tolerability of one SSRI to another.

Objective: The purpose of this trial was to compare the efficacy and tolerability of flexible doses of escitalopram with paroxetine in the long-term treatment of GAD.

Methods: In this randomized trial, patients with DSM-IV-defined GAD (baseline HAMA >= 18) received one week of single-blind placebo treatment, then 24 weeks of double-blind flexible-dose treatment with either escitalopram (10–20 mg/day) or paroxetine (20–50 mg/day), followed by a two week, double-blind, down titration period. Mean change from baseline to endpoint (LOCF) in HAMA scores was the primary efficacy variable.

Results: Mean baseline HAMA scores for the escitalopram (N=60) and paroxetine (N=61) groups were 23.7 and 23.4, respectively. Both escitalopram and paroxetine were associated with improvement in anxiety symptoms, with mean changes in HAMA scores from baseline to endpoint of −15.3 and −13.3, respectively (p=0.13). Tolerability measures appeared to favor escitalopram over paroxetine treatment. Significantly fewer escitalopram-treated patients withdrew from the study due to adverse events compared with paroxetine treatment (6.6% vs. 22.6%; p=0.02). Of adverse events reported by >20% of patients in either treatment group, diarrhea was reported twice as frequently by escitalopram treated patients, while ejaculation disorder, anorgasmia and decreased libido were reported at least twice as frequently by paroxetine treated patients.

Conclusion: These results suggest that escitalopram is as effective as paroxetine in the treatment of GAD, but with a more favorable tolerability profile, and support the use of escitalopram as a first-line treatment.

References:

Educational Objectives:
At the conclusion of this session, the participant should be able to appreciate that mood variability (rapid switching) may be a basic biological dimension of mood and anxiety disorders and that long-term treatment should address this. This is under-recognized because measurement of variability is more difficult than cross-sectional measures.
Conclusions: The core features of OCD are probably relatively independent of cultural variations. The sole exception to this rule seems to be the content of the obsessions, in which cultural factors may play a significant role.

References:

NR217 Monday, May 3, 3:00 p.m.-5:00 p.m.
Low-Resolution Electromagnetic Tomography and Treatment Response in OCD
Leonardo F. Fontenelle, M.D., Department of Psychiatry, IPUB-UFRJ, Rua Lopes Trovao 88 1501A Icaraí, Niterói, RJ 24220-071, Brazil; Mauro V. Mendlovicz, M.D., Isabela D. Soares, Ph.D., Juliana Kailaf, M.D., Pedro Ribeiro, Ph.D., Marci V. Versiani, M.D., Roberto A. Piedade, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize that findings from a new neuropsychological method, i.e., the Low Resolution Electromagnetic-Tomography, may help to predict response to drug treatment in OCD. The pretreatment 3D intra-cerebral distribution of neuronal electrical activity from the scalp-recorded potential distribution was assessed with the LORETA. Then, patients were treated with anti-OCD drugs employed in maximum tolerated doses for at least 12 weeks. The SPM99 T-Test for independent samples was employed to analyze the differences in the brain electrical activity, voxel-by-voxel, between responders and non-responders to drug treatment. The final result was a statistical map with the T-Test value for each voxel and its location in the brain, using the Talairach Atlas coordinates.

Results: Responders were characterized by significantly lower activities in beta band in the rostral anterior cingulate [Broadman’s area (BA) 24 and 32] in voxel (p = 0.02) and cluster-levels (p = 0.02). No other difference in the LORETA profile was find between groups.

Conclusions: Treatment response in OCD is associated with a distinctive pattern of electrical activity within the rostral anterior cingulate. A similar finding was already reported in treatment responders with major depressive disorder.

References:

NR218 Monday, May 3, 3:00 p.m.-5:00 p.m.
Specificity of the Somatic Symptoms of GAD
Iwona Chelminski, Ph.D., Department of Psychiatry, Rhode Island Hospital, 235 Plain Street, Providence, RI 02905; Mark Zimmerman, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to better understand the psychometric characteristics of the DSM-IV definition of GAD.

Summary:
Objective: Despite the prevalence of persistent and free-floating anxiety in many psychiatric patients, Generalized Anxiety Disorder (GAD) remains a controversial and poorly understood diagnostic entity. The diagnostic criteria had been changed in each of the DSM editions and poor choice of the required somatic symptoms in the DSM-IV definition is blamed for the low diagnostic reliability. Some assert that elevated muscle tension is the key somatic variable and suggest that it be a required criterion (Joormann and Stoeber, 1999). Others, argue that presence of at least four of the seven first-rank symptoms and one of the five second-rank symptoms would improve diagnostic consistency (Starcevic and Bogovejic, 1999). In the present study from the Rhode Island Methods to Improve Diagnostic Assessment and Services (MIDAS) project we examined the prevalence of the GAD physical symptoms in psychiatric outpatients presenting for treatment.

Methods: 770 outpatients were evaluated with the Structured Clinical Interview for DSM-IV and completed a self-report measure of frequency of physical symptoms. Sensitivity and specificity indices of the six GAD somatic symptoms were calculated. To address the question of which somatic symptom is the best predictor of the presence of GAD we also conducted logistic regression analysis.

Results: Fatigue and concentration difficulty were the most frequent symptoms in the GAD patients (70% and 69%), while muscle tension was the least common (48%). The sensitivity indices ranged from 48% to 70% and specificity from 42% to 69%. “Feeling keyed up or on edge” had the highest overall hit rate and the kappa coefficient. Likewise, in the logistic regression, of the six independent variables only this one was found significant.

Conclusion: Overall, psychometric properties of the GAD DSM-IV criteria are modest to poor. The present analysis suggests that “feeling keyed up or on edge” might be the most GAD specific somatic symptom.

References:

NR219 Monday, May 3, 3:00 p.m.-5:00 p.m.
Anxiety Hurts Too
Iwona Chelminski, Ph.D., Department of Psychiatry, Rhode Island Hospital, 235 Plain Street, Providence, RI 02905; Mark Zimmerman, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to better understand the relationship between pain and psychiatric conditions such as depression and anxiety.
Summary:

Objective: Somatic symptoms are common in the presentation of depressive syndromes. Fatigue, sleep problems, appetite changes are the three of the nine required DSM-IV criteria for major depressive episode. Many depressed patients also report in physical pain. While there is some evidence that chronic pain is not specific to depression (Sartorius et al., 1993), this question has not received much empirical study. In the present report from the Rhode Island Methods to Improve Diagnostic Assessment and Services (MIDAS) project we examined the specificity of the association between depression and complaints of physical pain.

Method: Eight hundred fourteen outpatients were evaluated with the Structured Clinical Interview for DSM-IV and completed measures of pain and physical symptoms. To address the question of specificity of pain and somatic complaints we compared four nonoverlapping groups of patients: (1) with a pure diagnosis of major depression (i.e., no comorbid anxiety, n=152), (2) with a pure diagnosis of any anxiety disorder (i.e., no comorbid depression, n=197), (3) with coexisting anxiety and depressive diagnoses (n=241), and (4) without either disorder (n=224).

Results: The patients without depression and without anxiety disorder reported significantly less pain and somatic symptoms that the other three groups. The pure diagnostic groups (i.e., pure anxiety and pure depression) did not significantly differ from each other on either measure. The total scores of the pain and somatic complaints measures were significantly higher in patients with both depression and anxiety than in patients with pure disorders or no anxiety and no depression.

Conclusions: Our results suggest that pain is not specific to depression. Anxiety, in the absence of depression also hurts, and in the presence of depression it hurts even more.

References:

NR220 Monday, May 3, 3:00 p.m.-5:00 p.m.
Social Phobia and Anxiety Inventory (SPAI) Validation in a Brazilian Sample
Patricia Picon, M.D., Psychiatry Department, Pucrs University, Rua Padre Chagas 415/803, Porto Alegre, RS 90570-080, Brazil; Gabriel J.C. Gauer, M.D., Gisele G. Manfro, M.D., Deborah C. Beidel, Samuel M. Turner

Educational Objectives:
At the conclusion of this session, the participant should recognize that the SPAI is a reliable instrument to be used in the U.S. as well as in Brazil.

Summary:
Objectives: The aim of this study is to examine the internal consistency, the test-retest reliability, and the confirmatory factor structure of SPAI Portuguese version in a Brazilian sample of university students.

Methods: After informed consent, SPAI Portuguese version was applied in a heterogeneous two-stage cluster sample of 1,014 Brazilian university students, both genders, from six different facul-
ities. Two weeks later it was readministered to 225 students.

Results: Twelve subjects were excluded due to incomplete questionnaire. After double entry data, the studied sample (213) demonstrated: Cronbach’s Alpha 0.98, Pearson Correlation Coefficient 0.83 (IC 95% 0.78-0.87, p<0.001) and Intraclass Correlation Coefficient 0.83 (IC 95% 0.78-0.87, p<0.001). The confirmatory factor analysis with varimax rotation in the original total sample (1,014) showed a two factor structure, social phobia and agoraphobia subscales, identical to the English version.

Conclusion: The internal consistency, the test-retest reliability and the factor structure were similar to the findings described in studies performed in American samples. The present study has shown that the Portuguese version of SPAI is a reliable and valid measure of social anxiety for Brazilian adults to screening individuals with probable social phobia.

Funding Source(s): Research Funding Brazilian Agencies; Fundação de Apoio à Pesquisa do Rio Grande do Sul (FAPERGS) and Fundo de Incentivo à Pesquisa do HC/UFRGS (FIFPE).

References:

NR221 Monday, May 3, 3:00 p.m.-5:00 p.m.
Escitalopram Efficacy in Clinical Subgroups in Social Anxiety Disorder
Supported by Lundbeck Pharmaceuticals
Dan J. Stein, M.D., Psychiatry Department, University of Stellenbosch, PO Box 19063, Tygerberg, SA 7505, South Africa; Elisabeth W. Andersen, Ph.D., Malcolm Lader, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to evaluate the efficacy of escitalopram versus paroxetine in six factors of the LSAS scale.

Summary:
Introduction: Escitalopram has demonstrated efficacy for the treatment of social anxiety disorder (SAD) in two placebo-controlled trials. A factor analysis of the primary efficacy parameter, the Liebowitz Social Anxiety Scale (LSAS), revealed six LSAS factors (strangers, eat/drink small group, public space, work, party), which were all responsive to treatment.

Methods: Each of the six subscale scores and 24 single items was analyzed separately, using observed cases, for the effect of escitalopram at week 24, using ANCOVA with treatment and center as factors and baseline subscale as covariate. Data were from a randomized, double-blind, 24-week trial in SAD, which included escitalopram 20mg (N=170), paroxetine 20 mg (N = 169), and placebo (N=166).

Results: Using a six-factor model, escitalopram 20 mg was numerically superior for factor 4 (public space), and statistically significantly superior to paroxetine 20mg for the other five factors (p<0.05). Escitalopram 20mg was more effective than paroxetine 20 mg on all of the single items, apart from item 18 (expressing disagreement or disapproval to people you don’t know very well). Conclusion: Compared with paroxetine, escitalopram is significantly more effective across most areas of disability in SAD.

Funding Source(s): This research was funded by H. Lundbeck A/S.

References:
Factors Analysis of the LSAS in SAD: Relationship to Disability Scores

Supported by Lundbeck Pharmaceuticals

Dan J. Stein, M.D., Psychiatry Department, University of Stellenbosch, PO Box 19063, Tygerberg, SA 7505; South Africa; Elisabeth W. Andersen, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to evaluate the efficacy of escitalopram versus placebo in six factors of the LSAS scale.

Summary:

Introduction: The Liebowitz Social Anxiety Scale (LSAS) rates 24 items for both anxiety and avoidance, resulting in 48 individual ratings. Several analyses of the LSAS have been published, but there is less on the relationship of LSAS factors to disability scores and treatment outcomes.

Methods: LSAS baseline data from three studies (N = 1704) were submitted to a factor analysis. Factors were identified using a maximum likelihood approach and rotated with a varimax rotation to ease interpretation. Analysis of covariance was used to assess the relationship of LSAS factors to disability scores and treatment outcomes.

Results: A six-factor model was chosen. The six factors were: (1) talking to or meeting strangers, (2) eating and drinking in public, (3) being center of attention in a small group, (4) functioning in a public space, (5) work, and (6) party. These factors were differentially associated with different areas of disability. Escitalopram was, however, significantly superior to placebo for all factors: factors 1, 2, 3, 4, 6 (p < 0.001) and factor 5 (p < 0.05) for both observed-case and last-observation-carried-forward analysis.

Conclusion: A six-factor model was supported by the distinctive association between the factors and different areas of disability. Nevertheless, this model did not predict differential response to escitalopram, which was significantly superior to placebo in all symptom clusters.

Funding Source(s): This research has been sponsored by H. Lundbeck A/S.

References:


FRONTAL-LOBE EEG ALPHA HYPACTIVITY AND DISSONANCE IN HARM-PHOBIC CHECKER OCD

Gary L. Hamlin, M.D., Gwen L. Zornberg, M.D., Jerri D. Brock, Ph.D., Kathy J. Tobias, M.D.

Educational Objectives:

At the conclusion of this session, the participant should improve participants' understanding of clinically meaningful subtypes of GAD, pregabalin's efficacy in treating GAD, and pregabalin's safety and tolerability across its dosing range.

Summary:

Objective: To evaluate the efficacy of pregabalin, an α2-δ ligand, in clinically relevant subtypes of generalized anxiety disorder (GAD).

Methods: Data were collected from placebo-controlled Phase 2/3 studies of pregabalin as treatment of DSM-IV GAD. All pregabalin dosage groups (200 to 600 mg/day) were combined to yield the analysis sample, N = 1282; female = 60%; mean age = 39.4 yrs; base HAM-A = 25.4. Subgroups analyzed included those defined by the following variables: gender, age, severity (HAM-A ≥ 26), subsyndromic depression (HAM-D > 15), severe somatic symptoms (HAM-A somatic factor ≥ 12), and severe insomnia. A Week 4/6 LOCF-endpoint analysis was performed with responders defined as those having ≥ 50% reduction in HAM-A total score.

Results: Responder rates were significantly higher for pregabalin than placebo among males (56% versus 39%; p < 0.001), females (51% versus 32%; p < 0.001), and the elderly (55% versus 27%; p < 0.02) and among patients with severe anxiety (61% versus 39%; p < 0.001), subsyndromic depression (49% versus 31%;
NR225  Monday, May 3, 3:00 p.m.-5:00 p.m.
A Novel Treatment for Premature Ejaculation: A Randomized, Controlled Trial

M. Jan Wise, M.R.C., Department of Adult Psychiatry, Imperial College, 97 Crewys Road, London NW2 2AU, United Kingdom; Mireia Pujol, M.R.C., Martin R. Baggaley, M.R.C., Michael Crowe, Ph.D.

Educational Objectives:
At the conclusion of the session, the reader should be able to identify premature ejaculation and be aware of the advantages of a novel approach to its treatment.

Summary:
Objective: Is a novel device for the treatment of PE as effective as cognitive-behavioral therapy (CBT)?
Method: A dual center study recruited patients from psychosexual clinics and local newspaper adverts. 72 people responded of whom 58 met inclusion criteria; six were unable to attend follow-up. A stratified randomisation technique allocated 52 patients to receive either the device or CBT. Patients were assessed for latency with the Golumbok Rust Inventory of Sexual Satisfaction at recruitment, end of therapy, and three months post-treatment.

The mean latency for colitus was 0.8 minutes for both groups at the beginning of the trial, at completion it was 8.8 minutes for the device group and 2.6 minutes for the control group. Independent t-test, not assuming equivalence of variance, t = p<0.002.

The GRISS subscales revealed no statistically significant differences between the two groups, except in the premature ejaculation subscale. There was no statistically significant difference at the beginning of the trial, at 8 weeks the mean rank score for the device group was 22.6, lower than that of the therapy group 30.40 [t = 3.607, p < 0.05]. At three months 22.38 compared to 30.62 [t = 3.965, p<0.05].

Conclusion: This device is worth further consideration.

References:

NR226  Monday, May 3, 3:00 p.m.-5:00 p.m.
Tadalafil Treatment of Erectile Dysfunction in Men on Antidepressants
Supported by Eli Lilly and Company

Robert T. Segraves, M.D., Department of Psychiatry, Case Western Reserve University, 2500 Metro Health Drive, Cleveland, OH 44109-1986; Ronald W. Stevenson, M.D., Jay Lee, M.D., Daniel J. Walker, Ph.D., Wei Wang, M.D., Ruth Dickson, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to understand the efficacy of tadalafil in the treatment of erectile dysfunction in men taking concomitant antidepressants.

Summary:
Objective: To evaluate tadalafil (1), a new treatment for erectile dysfunction (ED) with an extended duration of action, up to 36 hours post-dose, in men taking antidepressants.
Method: A integrated analysis of 11 double-blind, placebo-controlled trials identified 111 men, mean age 56 yrs (range, 27–78) receiving antidepressants and tadalafil 10 mg or 20 mg (n = 82), or placebo (n = 29). Efficacy was measured by the International Index of Erectile Function (IIEF) Erectile Function (EF) domain score (2), the Sexual Encounter Profile (SEP) diary, and a Global Assessment Question (GAQ).

Results: 80% tadalafil patients reported improvement in erections (GAQ) compared to 30% on placebo (p<.001). Tadalafil-treated showed significantly greater baseline-to-endpoint improvement on the IIEF EF score compared to placebo (endpoint: tadalafil, 22.5; placebo, 14.4; p<.001). Successful intercourse attempts at endpoint was also greater with tadalafil than placebo (p<.001). Adverse events were low in all treatment groups.

Conclusion: Tadalafil improved ED in patients taking antidepressant medications. Given the high prevalence of antidepressant-induced and depression-associated sexual dysfunction (2), and the efficacy of tadalafil for treatment of ED in this analysis, further studies of tadalafil in these patient groups are warranted.

Funding Source(s): Lilly ICO

References:

NR227  Monday, May 3, 3:00 p.m.-5:00 p.m.
Effects of Sildenafil Citrate on Ejaculatory Delay and Erectile Dysfunction
Supported by Pfizer Inc.

H. George Nurnberg, M.D., Department of Psychiatry, University of New Mexico, 2400 Tucker NE, MSC 095030, Albuquerque, NM 87131; Paula L. Hensley, M.D., Susan Paine, M.S., Carol Slonimski, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to reuptake inhibitor-associated ejaculatory delay and erectile dysfunction and the complicated relationship between the two.

Summary:
Objectives: Serotonergic reuptake inhibitor antidepressant associated sexual dysfunction (SRI-AASD) is complex, involving primarily disordered orgasm and arousal dysfunction. Although controlled trials of sildenafil citrate have demonstrated efficacy for treatment of erectile dysfunction (ED) due to various etiologies,
including SRIs, its effectiveness for ejaculatory delay (EJD) and orgasm delay is unclear. This report examines sildenafil treatment for SRI-AASD with a focus on ED, EJD, and their concurrence.

Methods: 90 men with major depressive disorder in remission, on stable-dose antidepressant, and SRI-AASD were randomized to receive sildenafil (50–100 mg) or placebo for six weeks. Subjects entered an open-label extension phase where they received sildenafil for 18 additional weeks. Outcome measures included the International Index of Erectile Function, UNM-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 for SD domain scores for both double-blind and open-label phases of 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 73% for ED without EJD, 33% for ED with EJD, 20% for EJD without ED, and 57% for total ED or total EJD (P<0.02).

Conclusion: SRI-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, form-frustne, common diathesis, complication, independent-interactive, or severity of conditions.

Funding Source(s): Sponsored by Pfizer Inc.

References:

NR229 Monday, May 3, 2004, 3:00 p.m.-5:00 p.m.
Romantic Obsession Among Men Who Have Sex With Men
James C. Sorrentino, B.S., Psychiatry Department, Mt. Sinai School of Medicine, Box 1230, 1 Gustave Levy Place, New York, NY 10029; Frederick Muench, M.A., Thomas Irwin, Ph.D., Jon Morgenstern, Ph.D., Milton L. Wainberg, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to use the Romantic Obsession Scale with confidence to identify individuals in their practice who are affected by romantic obsession. Also, the participant should be able to differentiate romantic obsession as a subtype of sexual compulsivity.

Summary:
Objective: The aim of this poster is to report on the psychometric properties of an instrument to measure romantic obsession (RO). RO has been described as intense preoccupations or behaviors revolving around love or romance that are channeled toward real or fantasized individuals or relationships. Though the notion of RO is evident in the self-help literature and popular media, there is limited empirical data on this construct and no known scales to assess this phenomenon.

Method: Participants were among 183 inner-city NYC men who have sex with men (MSM) identifying as being sexually compulsive (SC) and who completed a one-time sexual health assessment of Project SPIN.

Results: Preliminary results indicate that the RO scale is internally consistent (alpha = .90). The scale displays adequate convergent validity with scales of SC and adequately discriminates between respondents who endorsed RO as a problem and those who did not.

Conclusions: Though RO and SC are often conflated in the literature, early findings suggest that RO may represent a subtype of SC. Understanding RO as a distinct diagnostic entity has direct clinical significance for the practitioner. Salient descriptive features of RO endorsers will be highlighted and directions for future research will be discussed. This study is funded by the CDC.
Funding Source(s): Center for Disease Control and Prevention (CDC)

References:

NR230 Monday, May 3, 3:00 p.m.-5:00 p.m.
Assessing Self-Esteem, Confidence, and Relationships in Men With Erectile Dysfunction Treated With Sildenafil Citrate: Results From an International, Multicenter, Double-Blind, Placebo-Controlled Trial Supported by Pfizer Inc.
Vera Stecher, Ph.D., Pfizer Incorporated, 235 East 42nd Street, 235/471, New York, NY 10017; Sidney Glina, Joseph Cappelleri, Ph.D., Sandeep Duttagupta, Ph.D., Nancy Sherman, Richard Siegel, M.D., Li-Jung Tseng

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the value of assessing psychosocial manifestations (self-esteem, relationships, confidence) of erectile dysfunction and the correlations of changes in these psychosocial factors with changes in erectile function in patients treated with sildenafil for ED.

Summary:
Objective: To use the erectile dysfunction (ED)-specific Self-Esteem and Relationship (SEAR) questionnaire to assess changes in self-esteem, confidence, and relationships in men with ED following treatment with sildenafil.

Methods: A 12-week, double-blind, placebo-controlled, flexible-dose (25, 50, or 100 mg) international trial was conducted in men aged ≥18y with ED. Change scores for the five components (Sexual Relationship and Confidence domains, Self-Esteem and Overall Relationship subscales, Overall score) and the 14 items of the SEAR questionnaire and correlations of changes in SEAR components with changes in the erectile function (EF) domain of the International Index of Erectile Function (IIEF) were obtained.

Results: 149 (mean±SD age, 54±12y; mean ED duration, 4.7y) and 151 patients (mean±SD age, 56±11y; mean ED duration, 4.3y) received double-blind treatment with placebo or sildenafil, respectively. Sildenafil offered significantly greater improvements over placebo on all SEAR components and items (P<0.0001) and all five domains of the IIEF (P<0.0001). Correlations for changes in SEAR component with EF domain scores ranged from 0.65 to 0.78 (P<0.0001). The most frequent adverse events with sildenafil (vs placebo) were headache (14% vs 5%), flushing (10% vs 2%), and dyspepsia (5% vs 1%); one patient discontinued sildenafil due to a treatment-related adverse event (epigastric pain).

Conclusions: In men with ED, sildenafil produced significant improvements in self-esteem, confidence, and relationships; these changes correlated significantly with changes in the EF domain of the IIEF.

Funding Source(s): Study sponsored by Pfizer Inc.

References:
Absence of Sexual Dysfunction in Patients With MDD Treated With Gepirone Extended Release Supported by Organon Inc.

Anita L.H. Clayton, M.D., Department of Psychiatry, University of Virginia, 2955 Ivy Road, Northridge Suite 210, Charlottesville, VA 22903; Leonard R. de Rogatis, Ph.D., Neely Ivgy-May, Ph.D., Steven B. Hollander, M.D., John H. Simmons, M.D., Kimberly Boyle, M.B.A., Michael Gibertini, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant will be able to describe the effects of gepirone-ER compared with placebo and fluoxetine on the incidence of treatment-emergent sexual dysfunction.

Summary:
Introduction: Pharmacologic interventions for major depressive disorder (MDD) are often complicated by the incidence of significant treatment-induced SD. As many as 30% to 60% of patients receiving selective serotonin-reuptake inhibitors (SSRIs) experience SD. Not all antidepressants, however, cause SD.

Objective: To determine the effect of gepirone-ER, a 5-HT1 agonist with demonstrated efficacy for the treatment of MDD on sexual function (SF), based on sexual outcomes assessments from four completed placebo-controlled studies.

Methods: Of four completed studies, three (placebo-controlled) assessed sexual functioning using the Derogatis Inventory of Sexual Function—Self-Report (DISF-SR), and one (fluoxetine and placebo-controlled) utilized the DISF interview with formal diagnosis of DSM-IV sexual disorders.

Results: In all four studies, the DISF score improved during acute or long-term treatment with gepirone-ER, as compared with placebo. When sexual disorders were formally diagnosed, the percentage of subjects who had no sexual disorders at baseline, but who developed a treatment emergent sexual disorder, was 6.33% for subjects who received gepirone-ER, 7.69% for subjects who received placebo, and 25.74% for subjects who received fluoxetine.

Conclusions: In contrast to fluoxetine, gepirone-ER treatment is not associated with treatment-emergent sexual disorders. Furthermore, the quality of life as it relates to sexual function does not appear to be adversely affected by gepirone-ER treatment.

References:

Alcohol and Assaults: Results of an Intervention at Bars in Stockholm

Thor Norstrom, Ph.D., SOFI, Stockholm University, Stockholm S-106 91, Sweden; Sven Andreason, M.D., Eva Wallin, M.A.

Educational Objectives:
At the conclusion of the session, the participant should have some knowledge about the role of prevention for reducing alcohol-related violence in bars.

Summary:
Introduction: Much research suggests an association between intoxication and violence. Various intervention programs have been developed to reduce intoxication and violence in public drinking places, but few of these have been rigorously evaluated. The aim of this study was to estimate the effects on violent crimes of an alcohol prevention program in Stockholm, Sweden. The program included training in responsible beverage service for servers, and stricter enforcement of existing alcohol laws.

Methods: Since the intervention was confined to a geographically delimited part of Stockholm, the Central City, a quasi-experimental design was applied, using another part of the city as control area. The intervention period was January 1998 through June 2001. Data on police-reported violence during the period of January 1994 through June 2001 were analyzed through ARIMA modeling.

Results: During the intervention period, violent crimes decreased significantly by 20% in the intervention area, controlled for the development in the control area.
NR235  Monday, May 3, 3:00 p.m.–5:00 p.m.
Preparing Clinicians to Treat PTSD in the Wake of 9/11 Terrorism

Lawrence V. Amsel, M.D., Department of Psychiatry, Columbia University, 245 West 107th Street, 14-F, New York, NY 10025, Randall D. Marshall, M.D., Yuval Neria, Ph.D.

Educational Objectives:
At the conclusion of this session, participants will gain an understanding of the barriers to dissemination of evidence-based psychotherapies for PTSD in the wake of the terror attacks of 9/11, as well as interventional strategies that might help overcome these barriers.

Summary:
Purpose: In the wake of the terrorist attacks of 9/11, there has been an unprecedented public mental health campaign to encourage affected individuals to seek psychotherapeutic help. This assumes that the current mental health workforce is prepared to treat these problems. Yet, while cognitive-behavioral therapy (CBT) has been established as an evidence-based (EB) treatment for PTSD, the acceptance and practice of this EB psychotherapy among general community mental health clinicians is unknown, as is the effectiveness of training programs to disseminate these CBT treatments.

Methods: This study explored the baseline attitudes of community clinicians towards CBT for PTSD, as well as their post-training attitude changes and the likelihood of their adopting this treatment modality after a two-day training workshop. Subjects were 382 licensed community mental health clinicians presenting for training in CBT for PTSD in the wake of the events of 9/11.

Results: At baseline clinicians rated the CBT techniques of prolonged imaginal exposure, in vivo exposure, structured patient homework, and cognitive restructuring, significantly lower than that of familiar psychotherapeutic techniques (p<0.00 for each comparison). They also rated their own self-efficacy for utilizing these CBT techniques significantly lower than for traditional psychotherapeutic modalities (p<0.00). Moreover, they revealed a gap between the perceived benefits of these techniques and their ability to practice them, which did not exist for familiar psychotherapy techniques (p>0.00). At the end of the workshops, clinicians reported changes in multiple attitudinal dimensions: skills and motivation changed significantly more than beliefs, perceived barriers to implementation, or theoretical reservations about the treatment (p<0.01). Clinicians rated demonstrations of clinical technique higher than lectures or role-play on the dimensions of educational impact, motivation to adopt, and skill building.

Conclusions: Knowledge, by itself, does not change the clinical behavior. Dissemination efforts for CBT techniques must address issues of self-efficacy, motivation to adopt new therapies, and barriers to adoption, if appropriate treatment for the psychological complications of terrorism is to be made widely available.

References:

References:

NR236  Monday, May 3, 3:00 p.m.–5:00 p.m.
Vicarious Traumatization at a Manhattan Hospital a Year After the 9/11 Tragedy

Spencer Eth, M.D., Department of Psychiatry, St. Vincent’s Hospital and Medical Center, 144 West 12th Street, Room 174, New York, NY 10011; Gentie Quitangon, M.D., Steven Lascher, M.D., Deborah Rovine, M.D., Lea DeFrancisci, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize symptoms of vicarious traumatization and the variables that affect development of symptoms in mental health professionals who work with trauma victims.

Summary:
Introduction: In the aftermath of the terrorist attacks on September 11, 2001, large numbers of New York City residents developed psychiatric symptoms that warranted intervention by mental health professionals. This study examines a group of mental health professionals and the impact of working with 9/11 trauma victims.

Method: A survey was conducted in the department of psychiatry of a Manhattan teaching hospital located near the World Trade Center one year after the 9/11 terrorist attack. Participation was voluntary and anonymous. The following measures were administered: Personal Questionnaire, Impact of Events Scale, Compassion Fatigue Self Test, and Trauma Symptom Inventory. A total of 35 respondents participated in the study. Statistical analysis was conducted.

Results: Significant symptoms of therapists included anxiety, hyperarousal, intrusion, avoidance, irritability, depression, dissociation, sexual dysfunction, and tension reduction behaviors. Personal trauma history, symptoms of anxiety and depression prior to 9/11, and caseload of 9/11 rescue workers were implicated in increasing the likelihood of symptomatology. Increased individual supervision, married status, older age, and increased religious participation may mitigate development of symptoms.

Conclusion: Further studies are necessary to understand more fully the impact of the evaluation and treatment of victims of mass traumatic events on the emotional well-being of mental health professionals.

References:

NR237  Monday, May 3, 3:00 p.m.–5:00 p.m.
Outcomes of Psychiatric Inpatients With and Without Mild Traumatic Brain Injury

Magdalena A. Mateo, Ph.D., Nursing Department, Northeastern University, 360 Huntington Avenue, Boston, MA 02115; Carol A. Gid, Ph.D., Nancy Merrill
Educational Objectives:
At the conclusion of this session, the participant should be able to describe two outcome measures that are used to determine the differences in the hospital course of inpatients with/without a history of mild traumatic brain injury.

Summary:

**Purpose:** To compare psychiatric inpatients with/mild traumatic brain injury (MTBI): length of stay [LOS], number of psychiatric admissions, change from admission to discharge on Global Assessment Functioning (GAF).

**Methods:** Psychiatric inpatients (n = 54), 18 to 65 years, with Axis 1 diagnosis, history of MTBI were interviewed. Inpatients (n = 52), matched with MTBI cases: age (± 8 years), gender, diagnostic category, was identified (comparison group).

**Results:** Each group had 27 (50%) females, ages 18 to 59 (M = 34.9, SD = 10.8). Causes of MTBI: sports (21, 39%), motor vehicle accidents (15, 28%), falls (9, 17%), other (9, 17%). Regression modeling methods adjusted for matching were used to contrast groups. LOS was longer for MTBI cases (12.4 ± 9.4, range 4–48) than non-MTBI subjects (10.0 ± 8.6, range 3–43). Differences was statistically significant, after adjustment for matching (t(df=53) = 2.57, p = 0.013). When adjusted for baseline GAF, LOS difference remained statistically significant (t(df=53) = 2.14, p = 0.037). The number of psychiatric admissions was 19% higher for MTBI cases (t(df=53) = 2.24, p = 0.025). GAF change-from-baseline did not differ between the groups.

**Conclusions:** Data from this study suggest psychiatric inpatients with MTBI history differ in hospital course.

**Funding Source:** McLean Hospital Nursing Alumni Association Endowment Fund, Harvard Center for Neurodegeneration and Repair, Foundation of the American Association of Neuroscience Nurses.

References:

**NR238 Monday, May 3, 3:00 p.m.–5:00 p.m.**

**Donepezil Therapy Improves Behavioral Symptoms in Patients With Alzheimer’s Disease**

**Supported by Eisai, Inc. and Pfizer, Inc.**

**Jeffrey L. Cummings, M.D., Department of Neurology, UCLA/Reed Neurosciences Center, 710 Westwood Plaza, Los Angeles, CA 90095; Richard Zhang, Ph.D., Tom McRae, M.D.**

**Educational Objectives:**

- At the conclusion of this session, the participant should be able to recognize the efficacy and safety of donezepil for the treatment of severe neuropsychiatric symptoms in patients with mild to moderate Alzheimer’s disease.

**Summary:**

**Objective:** To evaluate the efficacy of donepezil treatment on behavioral symptoms in patients with mild to moderate Alzheimer’s disease (AD).

**Methods:** Non-depressed patients exhibiting behavioral problems (Neuropsychiatric Inventory (NPI) total score >5 at screening and NPI severity scores ≥2 in at least 2 domains) were enrolled. Patients received open-label donepezil 5 mg/day for four weeks and 10 mg/day thereafter. At Week 8, patients were randomized to receive placebo or the antidepressant sertraline (25–200 mg/day), in addition to donepezil. Efficacy measures were the NPI total and 12 item scores, Clinical Global Impression Severity (CGI-B) and Clinical Global Impression Improvement (CGI-I) subscales.

**Results:** Results reported are for the placebo group (n=121) who received only donepezil for 20 weeks (mean baseline NPI-12 score [±SD]) 31.4 (±15.6) mean baseline MMSE score [±SD] 17.5 (±4.61). At Week 20, NPI-12 and NPI-10 total scores had improved by +8.2 (P<0.0061: relative change 27.8%, effect size 0.82) and +7.2 (P <0.0001: relative change 28.7%; effect size 0.58). Significant improvement in CGI-S and CGI-I measures were observed at Week 20. Donepezil was well tolerated; 10.5% of patients discontinued due to adverse events.

**Conclusions:** Donepezil therapy improved behavioral symptoms in patients with mild to moderate AD and severe neuropsychiatric symptoms.

**Funding Source(s):** Eisai, Inc., Pfizer Inc.

References:

**NR239 Monday, May 3, 3:00 p.m.–5:00 p.m.**

**ADHD in Child and Adolescent Psychiatric Disorders: Gender and Subtype Relationship**

**Rubaba Ansañ, M.A., Psychiatry Department, Scarborough Hospital, 3030 Brichmount Road, Toronto, ON M1W 3W3, Canada; Atilla Turgay, M.D., David Ng, M.D., Llewelyn W. Joseph, M.D., Michael Schwartz, Ph.D., Nadeem Chaudhry, M.D.**

**Educational Objectives:**

- At the conclusion of this session, the participant should be able to describe the frequency and subtype differences of ADHD in non-ADHD psychiatric disorders.

**Summary:**

**Objective:** To compare ADHD comorbidity rates and subtypes in oppositional defiant disorder (ODD), conduct disorder (CD), dysthyemic disorder (DD), major depression (MD), and pervasive developmental disorder (PDD).

**Method:** This comparative-analytic study reviewed seven ADHD comorbidity studies abstracted/published by a Canadian ADHD clinic. In all studies, patients were assessed by a child psychiatrist according to DSM-IV criteria, DuPaul ADHD Rating Scale, Offord-Boyle Child Health Study, and/or Gadow-Sprafkin Rating Scales.

**Results:** The rates of ADHD found in psychiatric disorders of this sample included: CD (N=245): 89.00%; ODD (N=1717): 92.99%; Major Depression (N=375): 34.24%; Dysthyemic Disorder (N=240): 62.91%; Pervasive Developmental Disorder - if DSM-IV allowed ADHD in PDD- (N=216): 71.35%; ObsessiveCompulsive Disorder (N=59): 40.88%; Generalized Anxiety Disorder (N=518): 50.23%. Most ADHD patients with Conduct Disorder had ADHD Combined type or Hyperactive-Impulsive or Combined Type. ADHD Predominantly Inattentive Type was more closely associated with Major Depression, Dysthyemic Disorder and Generalized Anxiety Disorder (p<0.01).

**Conclusions:** ADHD was very common in all the psychiatric disorders studied. Early identification and treatment of ADHD may facilitate treatment of other comorbid disorders. This study examined a clinical population from a large metropolitan ADHD clinic; hence the frequency of ADHD and comorbidity rates seen in this sample may be higher than community samples.
References:
2. Turgay A. Treatment of comorbidity in conduct disorder. Directions in Psychiatry (23):137–149.

NR240  Monday, May 3, 3:00 p.m.–5:00 p.m.
ADHD Comorbidity in Psychiatric Disorder Subtypes and Gender Relationships
Rubaba Ansari, M.A., Psychiatry Department, Scarborough Hospital, 3030 Birchmount Road, Toronto, ON M1W 3W3, Canada; Attila Turgay, M.D., David Ng, M.D., Llewelyn W. Joseph, M.D., Michael Schwartz, Ph.D., Nadeem Chaudhry, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to describe the frequency and subtype differences of ADHD in non-ADHD psychiatric disorders

Summary:
Finding: Most patients (79.60%) had two or more disorders. Oppositional defiant disorder and conduct disorder were most common in ADHD (54.96%, 19.99% respectively). Other disorders included anxiety disorders, major depression, dysthyemic disorder, and pervasive developmental disorders (11.85%, 8.37%, 6.62%, 5.03% respectively). In all combinations (with the exception of PDD), statistically significant differences were observed in male-female ratios (p<0.025 for all). ADHD Combined Type and Hyperactive Impulsive Type were more common in dysthyemic disorder and major depression than any other disorders.

Conclusions: ADHD has high comorbidity risk for other psychiatric disorders for all age groups. It is essential that ADHD patients are carefully screened for comorbidities in order to determine the most suitable treatment/medication. Since this study examined a clinical population from a large metropolitan ADHD clinic, the frequency and variety of comorbid disorders reported may be different in community samples.

References:
2. Turgay A. Treatment of comorbidity in conduct disorder. Directions in Psychiatry (23):137–149.

NR242  Monday, May 3, 3:00 p.m.–05:00 p.m.
Comorbid PTSD Linked With Suicidality Among Veterans With Schizophrenia
Jennifer L. Strauss, Ph.D., HSRD, Durham VA Medical Center, Box 152, 508 Fulton Street, Durham, NC 27705; Patrick S. Calhoun, Ph.D., Christine E. Marx, M.D., Marian L. Butterfield, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to: (1) recognize that high rates of comorbid PTSD are reported for persons with schizophrenia spectrum disorder, and that comorbid PTSD is associated with lower overall functioning in this cohort; (2) recognize increased suicidality in persons with schizophrenia and comorbid PTSD; and (3) discuss the links between comorbid PTSD and suicidality in schizophrenia.

Summary:
Objective: Approximately 30% to 40% of persons with schizophrenia have comorbid posttraumatic stress disorder (PTSD). These individuals report lower quality of life, poorer health, higher use of health services, and may be at high risk for suicidality.

Methods: Participants were inpatient male veterans with a clinical diagnosis of schizophrenia or schizoaffective disorder (N = 185). Comorbid PTSD was assessed with the PTSD Checklist (PCL). Six-month history of suicidality (ideation, attempt or self-harm) was assessed with the Duke Mental Health Study Inventory.

Results: Seventy-eight patients (47.3%) met DSM-IV criteria for comorbid PTSD. Those with PTSD did not differ in age, race,
education, marital status, BPRS subscales, alcohol or drug use compared with those without PTSD. In comparative analyses, those with comorbid PTSD were more likely to report suicidal ideation \((n = 53\) versus \(n = 29\); Chi-square = 19.71, \(p < .0001\)), and the association of suicidal behaviors with PTSD approached significance \((n = 11\) versus \(n = 5\); Chi-square = 3.28, \(p = .07\)). PTSD remained significantly associated with increased suicidal ideation in an adjusted model that accounted for age, marital status and substance use.

Conclusion: Hospitalized veterans with schizophrenia and PTSD are at higher risk for suicidality than those without PTSD. Targeted interventions addressing suicide risk in this cohort are warranted.

Funding Source: Associate Investigator Award to the first author (on PCC02054), Department of Veteran Affairs to the first author; Research Career Development Award to the fourth author (RCD-0019-2), Department of Veteran Affairs.

References:

NR243 Monday, May 3, 3:00 p.m.–05:00 p.m.
Screening Practices for Adolescent Dating Violence
Larry K. Brown, M.D., Department of Child Psychiatry, Rhode Island Hospital, 593 Eddy Street, Providence, RI 02903; Celia M. Lescano, Ph.D., Erika Litvin, B.A.

Educational Objectives:
- At the conclusion of this session, the participant should become aware of screening items for dating violence, understand the frequency of dating violence among adolescents, and become familiar with protocols for dating violence screening.

Summary:
Objective: Increasing awareness among health care professionals has helped in the identification and confrontation of suspected dating violence. The investigation of such awareness of relationship violence among adolescents and within mental health settings has yet to be studied. This project assesses the screening practices of psychiatrists for intimate partner violence among adolescents in psychiatric treatment.

Methods: Members of the American Academy of Child and Adolescent Psychiatrists (AACAP) were invited to participate in a brief questionnaire regarding screening practices and identification of dating violence. The current sample included 817 completed surveys, 629 via the web and 188 via mail (overall return rate 32%).

Results: 83.9% of physicians reported having ever identified dating violence, 65.0% have done so within the past year. Routine, consistent screening of dating violence is reported less frequently than for suicide ideation, drug use and parental domestic violence. A multiple logistic regression, entering observed significant covariates, found that screening for partner violence among adolescents is strongly associated with screening for other risk behaviors.

Conclusions: Partner violence is associated with factors common among adolescents with psychiatric disorders. The data suggest that screening practices can be improved by the use of specific protocols and practices.

References:

NR244 Monday, May 3, 3:00 p.m.–05:00 p.m.
PTSD in Disaster Workers Following the World Trade Center Attack
JoAnn Difede, Ph.D., Department of Psychiatry, Weill Medical College of Cornell University, 525 East 88th Street, Box 200, New York, NY 10021; Frank Weathers, Ph.D., Nihal Jayasinghe, Ph.D., Jennifer Roberts, Ph.D., Pamela Leck, Ph.D., Judith Cukor, Ph.D., Michael Crane, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to identify the negative psychological sequelae of 9/11 and its aftermath in a population of utility workers. Specifically, the participant should be able to recognize the incidence of posttraumatic stress disorder and related disorders in this population and to conceptualize the role of occupational health departments following a disaster.

Summary:
Introduction/Hypothesis: Our principal aim was to determine the prevalence of PTSD and comorbid disorders in utility workers who were deployed to work at the World Trade Center (WTC) following the September 11th attacks.

Methods: 519 Consolidated Edison employees were screened between June and November 2002 as part of a mandatory medical evaluation organized by the Occupational Health Department of Consolidated Edison.

Results: Using the full DSM-IV criteria, the Clinician Administered PTSD Scale (CAPS) yielded PTSD prevalence estimates of 9.8%. The prevalence estimates was 14.8% when only two of three Cluster C symptoms were required and substantially larger for subsyndromal PTSD (defined as meeting criteria for 2/3 symptom clusters) at 23.5%. Post-hoc comparisons revealed significant differences between groups whereby the subsyndromal group had significantly higher scores on the Beck Depression Inventory, Brief Symptom Inventory, and PTSD Check List than did the non-PTSD group, and the PTSD group had significantly higher scores than did the subsyndromal group (p<.05 for all comparisons).

Conclusions/Discussion: These results suggest that PTSD is a significant public health problem in this population. Our results underscore the importance of establishing mandatory screening programs for disaster relief workers and conducting controlled clinical trials for the treatment of PTSD.

References:

NR245 Monday, May 3, 3:00 p.m.–05:00 p.m.
Domestic Violence, Self-Esteem, and Substance Dependence in Female Inpatients
Jennifer L. MacLaughlin, B.S., University at Buffalo, 51 Raintree Island, Apt. 8, Tonawanda, NY 14150; Carolyn M.
Young, M.D., Sheetal G. Sheth, B.A., Gregory E. Wilding, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should understand that female psychiatric patients are at an increased likelihood for domestic violence and substance dependence, and the potential ramifications of these issues on patient care.

Summary:

Objective: This study examines domestic violence, self-esteem and substance dependence in female psychiatric inpatients, exploring the hypothesis that female psychiatric inpatients are more likely to report a history of domestic violence experiences, substance dependence and lower self-esteem, as compared with nonpsychiatric female inpatients.

Methods: Domestic violence experiences, self-esteem and substance dependence were assessed in 89 general medical inpatients and 91 psychiatric inpatients in a case-control study. Female inpatients, hospitalized between May 2003 and September 2003 at the Erie County Medical Center, Buffalo, NY, were recruited and interviewed individually.

Results: Subjects were divided into three groups: subjects without a psychiatric history, subjects diagnosed with a mood disorder, and subjects diagnosed with a psychotic disorder. All endpoint analyses were adjusted for demographic variables. The three groups exhibited statistically significant differences with respect to self-esteem, alcohol dependence, drug dependence and domestic violence. Subjects with a psychiatric diagnosis tended to have lower self-esteem scores (p=0.0002), higher alcohol dependence scores (p=0.0802), and higher drug dependence scores (p=0.0026). Subjects with a psychiatric diagnosis also reported more frequent episodes of domestic violence. For all endpoints, differences between case and control groups were more pronounced in subjects with a mood disorder than for subjects with a psychotic disorder.

Conclusions: Patients with psychiatric disorders are at an increased risk for domestic violence and substance dependence.

References:


NR247 Monday, May 3, 3:00 p.m.-05:00 p.m.
Plastic Surgery: Psychosocial Aspects
Hamed Kabiri, M.D., Department of Surgery, Mercy Health System, 411 Dogwood Circle, Aston, PA 19014

Educational Objectives:

At the conclusion of this session, the participant should be able to: (1) demonstrate the knowledge of the type and the prevalence of the most commonly encountered psycho-social problems of plastic surgery patients; (2) recognize the possible unique concerns of Iranian plastic surgery patients; and (3) recognize the significance of seeking the aids of specialists in social sciences in medical groups responsible for the care of plastic surgery patients.

Summary:

Objective: The close link between the disciplines of plastic surgery and psychiatry necessitates recognition of psychosocial problems of patients cared for by plastic surgeons.

Methods: The study was carried out to analyze the psychosocial problems of patients requiring plastic surgery referred to the clinics of Tehran University of Medical Sciences. One hundred patients were randomly chosen from those referred during the summer of 1999. Data were collected using standard tests for studying patients' adjustment to illness and the impact of various social factors, and used standard instruments to study health and quality of life. Standardized tests were performed to detect depression and DSM-IV criteria were used for diagnosing posttraumatic stress disorder.

Results: The results not surprisingly showed that the majority of these patients had serious psychosocial problems. Of various statistically valid results, the prevalence of posttraumatic psychologic problems (94%), feelings of embarrassment, and aver- sion to publicity (61%) were of great significance. The results show that Iranian plastic surgical patients have unique concerns. For example, the effect of their appearance on arranging a desirable marriage proved of great importance.
NR248  Monday, May 3, 3:00 p.m.–5:00 p.m.
A Longitudinal Study of Young Adults With Adolescent Physical Abuse
Sandra J. Kaplan, M.D., Psychiatry Department, Northshore University Hospital, 400 Community Drive, Manhasset, NY 11030; Suzanne Sunday, Ph.D., David Pelcovitz, Ph.D., Victor Labruna, Ph.D., Suzanne Salzinger, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should have increased understanding of psychopathology of young adults who were physically abused during their adolescence, and of co-occurring disorders and functioning according to gender of adults who were physically abused as adolescents.

Summary:
Physical abuse during childhood has been associated with poor adult functioning. This study assessed lifetime psychopathology (from SCID I and II) in young adults who had been physically abused as adolescents. As part of an ongoing follow-up study, 45 young adults (age 22–31) participated from an adolescent abuse group (n=99) recruited 10–14 years ago from the NY State DSS abuse register from Nassau and Suffolk Counties of documented adolescent physical abuse. Comparison subjects (n=68) who participated in the original study were matched to the abuse group. Significantly more subjects in the abuse than the comparison group had at least one Axis I disorder (64.4% vs. 60.3%) and at least one Axis II disorder (31.1% vs. 13.2%), and had more co-occurring Axis I disorder (2.93 vs. 1.51). Subjects in the abuse group had more unipolar affective disorders (46.7% vs. 26.5%), anxiety disorders (37.8% vs. 17.7%), alcohol dependence (31.1% vs. 8.8%), drug dependence (42.2% vs. 13.2%), and conduct disorder symptoms than comparison subjects. Abuse group males had more antisocial personality symptoms. The persistence of impairment into young adulthood is remarkable in that the abuse subjects had generally experienced relatively mild levels of physical abuse as adolescents and came from largely middle class backgrounds.

References:
Hypothesis: Temperament predicts workplace stress significantly.

Methods: TEMPS-A and MPT were implemented with 1,214 Japanese company employees to measure, depressive, cyclothymic, hyperthymic, irritable, anxious, typus melancholicus and schizoid temperaments. NIOSH measured eight areas of workplace stress. Hierarchical multiple linear regression analysis was implemented to assess the effects of temperament, while controlling the effects by age, gender and job rank.

Results: The increments of the variance by temperament were highly significant at p<0.001 for all categories of workplace stress. Temperament accounted for an additional 8.6%, 10.2%, 9.1%, 5.5%, 9.2%, 5.1%, 6.4% and 3.0% of the variances for role conflict, role ambiguity interpersonal conflict perceived control, social support, variance in workload, skill underutilization and quantitative workload respectively. Depressive, cyclothymic, hyperthymic, irritable, anxious, typus melancholicus and schizoid temperament scores were significant predictors of the stress liability in 1, 3, 2, 5, 2, 2 and 2 areas. These temperament scores were significant predictors of the stress robustness in 2, 0, 5, 0, 1, 3 and 1 areas.

Conclusion/Discussion: Temperament predicts workplace stress highly significantly. The understanding of temperament should improve the mental health care for the company employees.

Funding Source(s): Kanto Medical Center

References:

NR251 Monday, May 3, 3:00 p.m.-5:00 p.m.
Difference in Heart Rate Variability Between Panic Patients and Controls
Jong-Min Woo, M.D., Psychiatry Department, Seoul Paik Hospital, 65 Jurdong-2-Ga Chung-Gu, Seoul 100-032, South Korea; Young-Hee Choi, M.D., Haye Young Yoon, M.A., Woo Yeon Cho, M.A.

Educational Objectives:
At the conclusion of this session, the participant should understand the evidence of autonomic dysfunction in panic disorder

Summary:
Objectives: This study is to assess the difference in autonomic nervous system function using heart rate variability (HRV) between patients with panic disorder (PD) and normal controls(NC).
Method: 82 PD patients and 82 healthy, age- and gender-matched controls were included in this study. We gathered five-minute, short-term HRV in a structured setting. Both time and frequency domain measures were calculated.
Results: Mean age of PD and NC was 34.0 and 34.8, respectively. Body mass index did not show significant difference. PD showed higher mean heart rate (73.62 vs. 70.22, t=-2.06, p<0.05) and HRV index (58.88 vs. 40.95, t=-2.47, p<0.05). SDNN, RMSSD, LF, HF were lower in PD but without statistical significance.
Conclusion: This results indicate decreased HRV in PD patients than normal controls. The analysis of HRV revealed an autonomic substrate for the symptoms of panic.

References:

NR252 Monday, May 3, 3:00 p.m.-5:00 p.m.
Preclinical Profile and Clinical Safety of S-Tofisopam: A Novel Homophthalazine
Supported by Vela Pharmaceuticals Inc.

Steven M. Leventer, Ph.D., Research and Development, VelaPharm, 3131 Princeton Pike, Building 4, Suite 216, Lawrenceville, NJ 08648; Robert Kucharik, John C. Keogh, Karen Raudibaugh, Deirdre O'Hara, R.N., Naidong Ye, Ph.D., Brian Speicher, Kevin L. Keim, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to better understand the mechanism and spectrum of action of the novel homophthalazine S-tofisopam.

Summary:
Background: S-tofisopam is the S-enantiomer of racemic tofisopam, a homophthalazine used extensively outside the United States to treat anxiety and disorders related to stress and autonomic dysfunction, including the symptoms of menopause. We explored the characteristics of S-tofisopam in a series of preclinical and clinical experiments.

Methods: The binding profile of S-tofisopam was examined in vitro. S-tofisopam was also tested in a series of animal behavioral models, including the elevated-plus maze, the water-immersion stress test, the glass bead test, the balloon distension test, the restraint-cortisol test, and the stress-induced hyperthermia test. In addition, we explored the effects of S-tofisopam on skin temperature in ovariectomized mice. Finally, the safety and tolerability of single doses of S-tofisopam were assessed in a randomized, double-blind, placebo-controlled, Phase I clinical trial in healthy volunteers.

Results: S-tofisopam is not active at most receptor binding sites, including the classical benzodiazepine binding site, but does bind to the 2,3-benzodiazepine receptor. S-tofisopam may modulate autonomic tone via interaction with these 2,3-benzodiazepine receptors, which are localized in subcortical brain regions, including the hypothalamus. Although it was not active in the elevated-plus maze in mice, S-tofisopam reduced stress-induced ulcer formation in the rat, decreased stress/stretch-stimulated colonic motility in the mouse, and reduced abdominal contractions induced by colonic stretch in the rat. S-tofisopam also elevated cortisol levels in mice, regardless of the presence or absence of stress, supporting the potential for S-tofisopam to affect the hypothalamic-pituitary-adrenal axis. S-tofisopam had a hypothermic effect in mice, both before and after stress, and reduced elevated skin temperature in ovariectomized mice, an animal model of menopause. In addition, single doses of up to 400 mg S-tofisopam were well tolerated in healthy human volunteers.

Conclusion: Preclinical studies suggest a novel mechanism of action and unique spectrum of activity for S-tofisopam, including significant activity in animal models of stress and menopause. In addition, S-tofisopam was well-tolerated in healthy human volunteers at single doses of up to 400 mg. These data support further study of the safety and efficacy of S-tofisopam in conditions characterized by stress, including anxiety-related disorders, and in the treatment of the most frequently reported symptom of menopause, the hot flash. A multiple-dose, Phase I clinical trial of S-tofisopam...
in healthy men and postmenopausal women is in progress, and Phase II clinical trials are planned.

**Funding Source(s):** Vela Pharmaceuticals Inc.

**References:**


**NR253**

**PTSD and Depression Two Years After the Terrorist Attack on the Pentagon**

Douglas A. Waldrop, M.D., Department of Psychiatry, USUHS, 4301 Jones Bridge Road, Bethesda, MD 20814; Thomas A. Grieger, M.D., Monica M. Lovasz

**Educational Objectives:**

At the conclusion of this session, the participant should be able to describe the rates of psychiatric illness and healthcare utilization in the Pentagon staff two years following the terrorist attack.

**Summary:**

**Objective:** This study examined the presence of PTSD and depression and rates of healthcare utilization in a sample of the Pentagon staff two years after the September 11 attack.

**Method:** Anonymous surveys were administered using the PEQ-9 and PCL-17 and questions regarding exposure to the attack, injuries sustained, and questions about healthcare and mental healthcare use before and after the attack.

**Results:** Those at the Pentagon on the day of the attack were more likely to endorse PTSD (OR=3.93, CI95=1.79-8.80, Wald X^2=11.57, P=0.001), but not depression compared with those at other sites. Those injured in the attack were more likely to endorse PTSD and depression (OR=8.14, CI95=3.53–18.80, Wald X^2=24.15, P<0.0005 and OR=4.3, CI9 5=1.50-12.37, Wald X^2=7.36, P=0.007) than those not injured. Rates of healthcare use and mental healthcare use increased after the attack and remained elevated in the second year following the attack. While 13% of the sample reported PTSD, only 36% of those were receiving ongoing mental health treatment. Seven percent reported depression. Of those, 37% were receiving ongoing mental health treatment.

**Conclusion:** Those present or injured during the attack on the Pentagon have higher rates of psychiatric illness two years later and most are not seeking mental health care.

**References:**


**NR254**

**Binge Eating and Overweight in a Nonclinical Population**

Jose C. Appolinaro, M.D., Department of Psychiatry, University of Rio de Janeiro, Viscconde de Piraja 550 CJ 2002, Rio De Janeiro, RJ 22410-001, Brazil, Kamile Siqueira, M.A., Rosely Sichieri, M.D.

**Educational Objectives:**

At the conclusion of this session, the participant should be able to recognize the importance of binge eating in obese subjects.

**Summary:**

**Objective:** To investigate the relationship between overweight and binge eating in a large non-clinical population.

**Methods:** Consumers of of shopping centers from five cities in Brazil (N=2,858) who participated in a overweight prevention program completed a self-report questionnaire on demographics, general health measures, and specific questions about binge eating (DSM-IV), childhood obesity, and leisure physical activity. Body weight and stature were measured to calculated body mass index.

**Results:** The prevalence of binge eating (subjects who binged one or more times per week over the last three months) was 4.6% in men and 4.8% in women, respectively. Binge eating was significantly associated with overweight/obesity. In normal weight individuals, binge eating prevalence was 1.4% for men and 3.9% for women; in overweight/obese individuals, this prevalence was 6.5% and 5.5%, in men and women respectively (p<0.01). After adjustment for age, socioeconomic variables, and cities, those who reported binge eating had an odds ratio of being overweight/obese of 3.55 (95%CI:1.23-10.3) for men and 1.66 (95%CI:1.03-2.72) for women.

**Conclusion:** These findings suggest that episodes of binge eating may be a relevant risk factor for overweight/obesity.
artificially sweetened products may be an index of appetitive drive in this population.

Funding Source(s): MH 042206-16 psychobiology of eating behavior in eating disorders

References:

NR256 Monday, May 3, 3:00 p.m.-5:00 p.m.
Anorexia Nervosa and Quetiapine: Effect on Weight and Psychopathology Supported by Astra Zeneca Pharmaceuticals LP

Pauline Powers, M.D., Department of Psychiatry, University of South Florida, 3515 East Fletcher Ave, Tampa, FL 33613-4708; Yvonne Bannon, M.S., Rebecca Eubanks, R.S.C.

Educational Objectives:
At the conclusion of this session, the participant should be able to: (1) identify the type of psychotic symptoms that may be present in anorexia nervosa; and (2) assess the effects of quetiapine in anorexia nervosa patients.

Summary:
Objectives: The study was conducted to determine if quetiapine administered over a 10-week period in patients with anorexia nervosa resulted in weight gain or improvement in psychopathology.

Method: Fourteen patients with DSM-IV anorexia nervosa (either restricting or binge-purge subtype) who were between 15% and 25% below ideal body weight signed informed consent forms. At baseline and Week 10 (or early termination) the Eating Disorder Inventory-2 (EDI-2), Hamilton Depression Rating Scale (HAM-D), and State Trait Anxiety Inventory (STAI) were completed, and the Yale Brown Cornell-Eating Disorder Scale (YBC-EDS) and Positive and Negative Syndrome Scale (PANSS) were administered. Patients were seen weekly to assess clinical status, determine weight and vital signs, and evaluate for possible adverse events.

Results: At Week 10 patients had gained a mean of 2.59 pounds. There were statistically significant improvements in the HAM-D, the STAI, and certain subscales of the YBC-EDS. There were no statistically significant changes in the PANSS or EDI-2.

Conclusions: Although the weight gain was modest, the significant improvements in symptoms of depression and anxiety are likely to facilitate the comprehensive treatment of anorexia nervosa with quetiapine.

Funding Source(s): AstraZeneca

References:

NR257 Monday, May 3, 3:00 p.m.-5:00 p.m.
Childhood Trauma and Eating Disorders

Ana M. Garcia de Amurugu Bar, M.D., Department of Psychiatry, Hospital Italiano, Pje. M Padilla 4065, Buenos Aires 1430, Argentina; Cecilia de Simone, M.D., Carlos A. Finkelsztein, M.D., Viviana E. Horigian, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize the importance of taking into account childhood trauma in the treatment of eating disorders patients.

Summary:
Objective: to evaluate the frequency of childhood sexual abuse (CSA) and family violence (FV) in patients that consulted the Eating Disorders Department at the Hospital Italiano of Buenos Aires.

Method: 440 patients were interviewed and diagnosed according to the DSM IV criteria. CSA was considered as every historical experience of a sexual kind that included physical contact with a child. Voyeurism, exhibitionism, and covert sexual abuse were excluded. Family violence was considered as direct or indirect physical abuse (eg: throwing objects) against a child or at any other member of the family in child’s presence. Psychological abuse was excluded.

Results: 340 patients met criteria for E.D. (group I, 332 females, 8 males mean age: 22.9 years). The other 100 patients (group II, 93 females, 7 males, mean age: 23.9 years) met criteria for other psychiatric disorders. In group I, 13.2% had a history of CSA and 28.5% of FV. Both were more frequent in bulimic patients. In group II, the frequency of CSA was 5% and FV 14%.

Conclusions: Childhood traumatic experiences may increase the vulnerability to suffer from ED, especially bulimia nervosa. Differences between group I and II were significant for ASI (p < 0.05) and F.V. (p = 0.05).

References:

NR258 Monday, May 3, 3:00 p.m.-5:00 p.m.
Empirical Support for an Attachment Hypothesis of Eating Disorders

Marc A. Lindberg, Ph.D., Department of Psychology, Marshall University, 1 John Marshall Drive, Huntington, WV 25755-2672; Megan Thomas

Educational Objectives:
At the conclusion of this session, the participant will be better able to understand and diagnose specific attachment, family, and related personality characteristics associated with eating disorders.

Summary:
Objective: Because parent relationship have been shown to contribute significantly to the development of eating disorders (Smolak, Levine, & Striegel-Moore, 1996), different populations and definitions of eating disorders were examined with the Attachment and Clinical Issues Questionnaire (ACIQ). The ACIQ is a new 29 scale instrument with average alphas of .79, malingering scales, and extensive validity testing (Linberg & Thomas, 2003).

Method: Study 1 compared 23, 40-year-old females being treated for eating disorders in out-patient settings with 297 controls matched on age, socioeconomic status, and sex. Study 2 used 350 male and female high school and college students, using an eating disorder inventory (Gold, 2003).

Results: In Study 1, a discriminate function analysis found that the Family Suppression of Feelings, Shame, Sexual Intimacy, Denial, and Abuser scales served as the best discriminates between the two groups F (5, 293) = 19.67, p = .001 Further t-tests
found significant differences on 19 scales (Ambivalent, Avoidant, and Secure attachments to mother, father, and partner, Anger, Anxiety, Denial of Feelings, Control, Preoccupied Thinking, Family Suppression of Feelings, Peer Relations, Shame, Sexual Intimacy, Mistrust, and Withdrawal.) In Study 2, 16 of the same 19 scales significantly correlated with the eating disorder inventory in the same predicted directions.

Conclusion: The two different populations defined in very different ways converged on the same results, but the ACIQ was able to diagnose important individual differences that are clinically important.

**Funding Source(s):** Marshall University

**References:**

**NR259**

**Monday, May 3, 3:00 p.m.-5:00 p.m.**

**Validation of the Spanish Version of the SCOFF Questionnaire**

Javier Garcia-Campayo, M.D., Department of Psychiatry, Miguel Servet Hospital, Isabel La Católica 1, Zaragoza 50009, Spain; Concepcion Sanz Carrillo, M.D., Salvador Lou, M.D., Jose Antonio Ibanez, M.D., Victor Solano, M.D.

**Educational Objectives:**
At the conclusion of this session, the participant will be able to demonstrate the utility of the SCOFF questionnaire for the screening of eating behavior disorders in Spanish patients.

**Summary:**
**Objective.** To assess the performance of the Spanish version of a new screening tool (the SCOFF) for the detection of eating disorders in primary care settings.

**Methods:**
1. SCAN was used as gold standard comparison measure. Blinding was applied to administration of the SCOFF and the clinical interview.
2. Primary care patients, from six primary health care centers in Aragon, Spain, with probable diagnosis of eating disorder. Participants, 203 female patients between 15–53 years.
3. Main outcome measure: Validity as assessed by sensitivity, specificity, positive predictive value and negative predictive value.
4. In addition, test-retest reliability and the receiver operating characteristics (ROC) curve were calculated.

**Results:**
The best threshold point in the Spanish version is also 2+ positive answers as it was in the original British version. This cut-off point gives a sensitivity and a specificity for the detection of eating disorders in primary care of 97.7% and 94.4% respectively. The intraclass correlation coefficient was 0.97. In the ROC curve the area under the curve was 0.947.

**Conclusion:**
The SCOFF questionnaire shows excellent psychometric properties for the detection of eating disorders in primary care in Spanish population and it deserves to be systematically used in at risk population.

**References:**

**NR260**

**Monday, May 3, 3:00 p.m.-05:00 p.m.**

**Anticonvulsants in Pregnancy: Practices of Neurologists Versus Psychiatrists**

Adele C. Viguera, M.D., Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street/WACC 815, Boston, MA 02114; Lee S. Cohen, M.D., Alison Remnick, B.A., Edward Bromfield, M.D., Giselle A. LeBlanc, B.A., Rachel Bender, John Hennen, Ph.D.

**Educational Objectives:**
At the conclusion of this session, the participant should be able to recognize differences in attitudes and practices among neurologists and psychiatrists who care for pregnant women treated with anticonvulsants.

**Summary:**
**Introduction:** Anticonvulsants are used in the treatment of neurological and psychotropic disorders. While there exist consensus guidelines on the use of anticonvulsants in neurology in childbearing women, there are no uniform consensus guidelines in psychiatry for women who are treated with anticonvulsants for primary affective disorders. The objective of this study was to assess attitudes and practices regarding use of anticonvulsants in childbearing women among neurologists and psychiatrists.

**Method:** A survey was sent to a random sample of 300 physicians. A total of 160 questionnaires were sent back completed including: 34 general psychiatrists, 39 psychiatrists specializing in women’s mental health, 40 general neurologist, and 47 neurologists specializing in epileptology.

**Results:** The overall response rate was 53%. Psychiatrists and neurologists were similarly likely to refer their patients for pre-pregnancy consultation, recommend folic acid supplementation, and inform women of childbearing potential of the teratogenic effects of anticonvulsants. However, the specialties differed significantly in attitude and clinical practice in managing pregnant women on anticonvulsants. Overall, neurologists endorsed having a positive to extremely positive attitude toward women planning pregnancy and breastfeeding on anticonvulsants compared to psychiatrists (p<0.004). Psychiatrists felt it was extremely important to inform patients of potential risks of neonatal toxicity and long-term neurobehavioral effects of in-utero exposure to anticonvulsants compared to neurologists (p<0.006). With respect to breastfeeding, psychiatrists were more likely than neurologists to discuss as well as recommend specific infant monitoring for potential risks of liver toxicity. (p<0.001), hematological effects (p<0.003), and long-term neurobehavioral effects (p<0.001) compared with neurologists who rarely recommend specific monitoring for infants exposed to anticonvulsants through breast milk.

**Conclusions:** Based on their self-reports, psychiatrists and neurologists differed significantly on the management of pregnant women on anticonvulsants. This survey demonstrates the need for evidence-based guidelines for the use of anticonvulsants in women of reproductive age.

**Funding Source(s):** Stanley Center Grant, NIMH K23 MH1609

**References:**
NR261  Monday, May 3, 3:00 p.m.–5:00 p.m.
Mammography Anxiety in a Community Outreach Program
Jane Brown Sofair, M.D., Department of Psychiatry, Atlantic Health Systems, 52 Maple Ave, Morristown, NJ 07960-5216; Martha Lehlbach, R.N.C.

Educational Objectives:
At the conclusion of this session, the participant should be able to: (1) recognize the uncertain role of worry in mammography compliance, with a focus on women of colombian background; (2) understand facilitators and barriers to mammography adherence; and (3) review preliminary longitudinal pilot data on anxiety levels in a sample of women undergoing mammography in a hospital-sponsored community outreach program.

Summary:
Studies reveal that anxiety is a double-edged sword in mammography adherence. Mammography worry among women of minority/immigrant status has been underdocumented, possibly due to access, cultural and/or translational factors. Hispanic women have lower breast cancer incidence rates than non-Hispanic white and black women and tend toward advanced stage diagnosis, even when controlling for screening frequency. Therefore, it is important to evaluate any potential compliance barriers.

This longitudinal pilot study of 26 women in a community outreach program (61% of Colombian origin, 77% non-insured) examined pre- and post-mammography anxiety levels to assess a hypothesized reduction in worry that would promote returning for a future mammogram. Structured questionnaires and the SCL-90-R Symptom Checklist were utilized, in Spanish where appropriate. Paired T-tests and frequencies were calculated in SPSS.

Global Severity Index (GSI) T-scores dropped, on average, four points after completion of mammograms (p = 0.001), a pattern not upheld for the Anxiety Symptom Dimension. Seven subjects reported feeling more upset after the mammogram, as reflected on at least one research question. Ninety-one percent reported intent for future mammograms.

Increased post-procedural upset deserves further study. The high percentage of intended future compliers may reflect the effectiveness of the hospital outreach program.

Funding Source(s): Morristown Memorial Health Foundation

References:

NR262  Monday, May 3, 3:00 p.m.–5:00 p.m.
Childcare and Social Support Modify the Impact of Maternal Depression
Li-Ching Lee, Ph.D., Bloomberg School of Public Health, Johns Hopkins University 615 N. Wolfe Street, Room E6516 Baltimore, MD 21205; Carolyn T. Halpem, Ph.D., Sandra L. Martin, Ph.D., Irva Hertz-Picciotto, Ph.D., Chirayath M. Suchindraw, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to carry out more effective treatment plans for childbearing women with depressive symptoms.

Summary:
Objective: To investigate the presence and patterns of modification effects of child gender, social support, and child-care on the relationship between maternal depression and child behavioral problems at two child developmental stages.

Method: A total of 1,216 families drawn from 10 locations across the United States, whose mothers were age 18 or older at the time of the study child birth and who had completed outcome measures, child internalizing and externalizing behavioral problems, for at least one follow-up time point (24-months, 36-months).

Results: Results from Generalized Estimating Equation (GEE) analyses, which allow time-dependent and time-independent predictors in models, indicated that social support was a significant effect modifier in the associations between externalizing behavioral problems and maternal depression (p<.05). The provision of child-care from other caregivers emerged as a significant effect modifier in associations between internalizing behavioral problems and maternal depression (p<.05).

Conclusions: Social support mitigated the associations between maternal depression and child externalizing behavioral problems; however, the protective effect decreased as the severity of maternal depression increased. On the other hand, child-care provided by other people reduced the associations between maternal depression and child internalizing behavioral problems.

References:

NR263  Monday, May 3, 3:00 p.m.–5:00 p.m.
HRT and SSRI Prescription Patterns: An Inverse and Reciprocal Relationship
Roger S. McIntyre, M.D., Department of Psychiatry, University of Toronto, 399 Bathurst Street, Toronto, ON M5T 2S8, Canada; Jakub Z. Konarski, M.S.C., Sophie Grigoriadis, M.D., Nancy Fan, Ph.D., Deborah Mancini, M.A., Kari Fulton, B.A., Donna E. Stewart, M.D., Sidney H. Kennedy, M.D.

Summary:
Context: The antidepressant effects of hormone replacement therapy (HRT) are conjectured from the available data. The use of serotonergic antidepressants for menopausal symptoms is established. Prescription patterns for these foregoing classes of medications are surmised to be interdependent. This ecological investigation attempts to correlate changes in HRT prescriptions with changes in selective serotonin reuptake inhibitors (SSRIs) prescriptions in Canada's most populous province (Ontario).

Methods: A private prescriptions claim database was scrutinized for trends in HRT and SSRI prescriptions from January 2001 to July 2003 inclusive. Gender and age-adjusted data were available for analysis. Main outcome measures included the number of prescriptions dispensed for HRT and SSRIs, further augmented with a regression model predicting SSRIs prescription pattern based on HRT utilization.

Results: An abrupt decrease in HRT prescriptions was noted along with a rapid and reciprocal increase in prescription for SSRIs therapy. These changes temporarity coincided with media attention to the deleterious effects of HRT in July 2002. HRT and SSRIs prescription rates were closely correlated. HRT prescription rates predicted SSRIs prescription rates pre and post July 2002, with HRT prescription increases and decreases coinciding with concomitant inverse SSRIs decreases and increases respectively.
 Polycystic Ovarian Syndrome Is Associated With Valproate Use in Bipolar Women

**Supported by NIMH and Abbott Laboratories**

Hadine Joffe, M.D., Psychiatry Department, Massachusetts General Hospital, 15 Parkman Street, WACC 812, Boston, MA 02114; Lee S. Cohen, M.D., Trisha Suppes, M.D., Wren L. McLaughlin, B.S., Judith M. Adams, D.M.U., Francine J. Molay, M.S.W.; Janet E. Hall, M.D., Gary S. Sachs, M.D.

**Educational Objectives:**

At the conclusion of this session, the participant should be able to understand the relationship between valproate use and treatment-emergent PCOS in women with bipolar disorder.

**Summary:**

**Objective:** To compare the incidence of polycystic ovarian syndrome (PCOS) after initiation of valproate versus other mood stabilizers and the prevalence of ultrasound-defined polycystic ovarian morphology (PCOM) in valproate and non-valproate users among women with bipolar disorder.

**Method:** 299 women with bipolar disorder were evaluated for evidence of PCOS and PCOM at 16 Systematic Treatment Enhancement Program for Bipolar Disorder sites. PCOS was defined by infrequent menses (<9 in past year) and hyperandrogenism. After excluding women with PCOS predating mood-stabilizers, hyperprolactinemia, and hormone use, 228 women were evaluable for treatment-emergent PCOS. 224 women were evaluable for PCOM.

**Results:** Subjects (age 33.1 ± 7.3 years) evaluable for PCOS included 86 valproate-users and 142 non-users (64 lithium, 51 lamotrigine, 29 topiramate, 26 gabapentin, 15 carbamazepine, 11 oxcarbazepine). Nine (10.5%) valproate-users versus two (1.4%) non-users (one lamotrigine, one gabapentin) had treatment-emergent PCOS (relative risk 7.4, 95% CI 1.6-33.6, p = 0.003). PCOS developed within one year of valproate use and was associated with an increased body-mass index (p = 0.01). PCOM was seen in 43 (52.4%) valproate-users and 58 (47.9%) non-users (p = 0.51).

**Conclusions:** PCOS occurs more frequently after initiation of valproate than other mood-stabilizers, without an increased prevalence of PCOM. Attention to reproductive-system characteristics is important in managing women with bipolar disorder.

**Funding Source(s):** Co-sponsored by the NIMH contracts (Massachusetts General Hospital, University of Pittsburgh, and University of Texas, San Antonio) and Abbott Laboratories, Inc.

**References:**


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**NR265**

**Monday, May 3, 3:00 p.m.-5:00 p.m.**

**Impact of Escitalopram Versus Hormone Therapy on Symptomatic, Menopausal Women Supported by Forest Laboratories, Inc.**

Claudio N. Soares, M.D., Department of Psychiatry, Mass General Hosp. Center for Women’s Health, 15 Parkman Street, WAC 812, Boston, MA 02114; Helga C. Arsenio, B.S., Paolo Cassano, M.D., Lee S. Cohen, M.D.

**Educational Objectives:**

At the conclusion of this session, the participant will recognize the efficacy of using antidepressants compared with hormone therapy for the treatment of menopause-related physical and depressive symptoms.

**Summary:**

**Background:** The menopausal transition has been associated with an increased medical and psychiatric morbidity, affecting quality of life and social functioning. Given the recent controversy involving the use of hormone therapy (HT), novel treatment options are needed.

**Objective:** This preliminary report examined the efficacy of escitalopram compared with HT for the treatment of peri and postmenopausal women suffering from depressive disorders and menopause-related symptoms.

**Methods:** Twenty-six women aged 40–60 years (11 peri, 15 postmenopausal) with depressive disorders (M.I.N.I. interview) and menopause-related symptoms (Greene Climacteric Scale scores, GCS) were randomly assigned to receive an 8-week open treatment with escitalopram (10–20 mg/day) or HT (ethinyl estradiol, 5mcg/day; norethindrone acetate, 1mg/day). Symptoms were assessed at baseline, 2, 4 and 8 weeks. Overall remission was defined as remission of depression (a score of < 10 on the Montgomery-Asberg Depression Rating Scale- MADRS), AND remission of menopause-related symptoms, (50% decrease in GCS total scores, with vasomotor sub-scores <3). Changes in quality of life were assessed by the MENOQOL questionnaire.

**Results:** Twenty-two women (12 on HT, 10 on escitalopram) were included in the analyses (LOCF). Both groups showed significant improvement in MADRS, GCS, and MENOQOL scores (p<0.05 for all comparisons, Mann-Whitney tests). Remission of depression was observed in 70% of women on escitalopram, compared to 25% treated with HT (p=0.03, Pearson chi-square test). Remission of menopause-related symptoms was noted in 60% and 46% of women, respectively (p=0.21). Overall remission occurred in 50% of women on escitalopram, and in 16.7% on HT (p=0.09).

**Conclusions:** Escitalopram showed superior efficacy compared to HT for the treatment of depression in peri and postmenopausal women. In addition, the use of escitalopram resulted in significant improvement in physical symptoms and quality of life, and may constitute an interesting treatment option for women who are unable or unwilling to receive treatment with HT.

**Funding Source(s):** Forest Laboratories, Inc./NARSAD

**References:**


NR266  Monday, May 3, 3:00 p.m.-5:00 p.m.
Adequacy of Antidepressant Treatment During Pregnancy
Sheila Marcus, M.D., Department of Psychiatry, University of Michigan, 900 Wall Street, Riverview Building, Ann Arbor, MI 48109-0722; Lisa S. Seyfried, M.D., Heather A. Flynn, Ph.D.

Educational Objectives:
Clinicians reviewing this research will become familiar with the high rates of depressive symptoms that persist in pregnancy, as well as suboptimal prescribing patterns that may contribute to these elevated mood symptoms.

Summary:
Study Aims: This study focused on women taking antidepressants (SSRIs) during pregnancy, their adequacy of use, and relationship to depressive symptomatology in women seeking obstetrics care.
Methods: 275 women at risk for depression based on screening in obstetrics (using CESD cutoff of ≥ 16) completed diagnostic interviews to determine depression status and history (SCID), severity (BDI-II), and use of antidepressant medications.
Results: 13% of women overall (n=36) reported any use of medications for depression, 25% of whom met criteria for current MDD. Among women who reported using antidepressant medication during pregnancy, most (70%) also continued to have elevated depressive symptoms. Less than half (44%) of the women taking antidepressants reported minimally adequate dosage (defined as ≥ 20 mg fluoxetine, or ≥ 50 mg sertraline, ≥ 150 mg venlafaxine, bupropion) and duration (≥ 12 weeks daily) of medication use.
Conclusions: Women using antidepressants during pregnancy demonstrate depressive symptoms, suggesting suboptimal management. Future studies should stress adequacy of treatments prescribed and monitoring adherence to recommended treatments. Full symptom remission should be the goal for antenatal and postnatal depression in order to minimize risk to mother and baby.

Funding Source(s): University of Michigan Health Systems

References:

NR267  Monday, May 3, 3:00 p.m.-5:00 p.m.
Effect of Remission of Depression on Personality Traits in a Community Clinic
Brady G.S. Case, M.D., Psychiatry Department, NYU School of Medicine, 1 West 72nd Street, #46, New York, NY 10023; Matthew G. Biel, M.D., Eric D. Peselow, M.D., Mary Anne Pressman, M.D., Mary T. Guardino, B.A.

Educational Objectives:
To evaluate personality traits during depression and following clinical recovery so as to get a better understanding of the relationship between personality traits and clinical symptoms.

Summary:
Objective: With research showing a 30% to 70% prevalence of personality disorders in samples of depressed individuals, there is clear evidence for the comorbidity of personality disorders and unipolar depression. One major issue is the difficulty in making a diagnostic distinction between an actual personality disorder and the concomitants of an acute clinical state. For instance, it has been shown that patients describe themselves as having more abnormal personality traits during periods of acute psychopathology. It is the purpose of this poster to evaluate self-reports of patients individual personality traits during depression and following clinical recovery.
Method: Over a 10-year period, we measured personality traits/disorder in 168 patients during acute depression and following clinical recovery. We used the Structured Interview for DSM-IV Personality Disorder (SIDP) was used to measure maladaptive personality traits. The SIDP measures ratable traits of the 10 DSM-IV personality disorders. All traits within a disorder are rated on a 0-3 point scale.
Results: All dimensional DSM-IV personality disorder scores with the exception of antisocial decreased upon clinical recovery. The total personality dimensional score was 23.79 during depression vs 22.05 upon clinical recovery (t=5.19 p<.0001). During depression 95/168 (56.6%) met criteria for at least one personality disorder vs 73/168 (44.5%) during clinical recovery.
Conclusions: For six of the 11 DSM-III disorders (all Cluster A and all Cluster C except passive-aggressive) personality trait scores significantly diminished during euthymic mood.

References:

NR268  Monday, May 3, 3:00 p.m.-5:00 p.m.
Use of Medication in Hospitalized Patients With BPD
Thomas A. Grieger, M.D., Department of Psychiatry, Uniform Services University Health System, 4301 Jones Bridge Road, Bethesda, MD 20814; Percival L. Cueto, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize patterns of pharmacologic treatment utilized for symptoms in hospitalized patients with borderline personality disorder.

Summary:
Objective: This study assesses the nature of medications used off label with patients hospitalized with borderline personality disorder compared to age and gender matched hospitalized psychiatric controls.
Method: Hospitalization records from July 2000 and July 2002 were retrospectively reviewed. Patients with a diagnosis of bipolar disorder, psychotic disorder, and anxiety disorders were excluded. 147 patients had a diagnosis of borderline personality disorder. These patients were matched by gender, age, and day of admission with other hospitalized patients. Pharmacy records were examined for medications prescribed at discharge. Rates of prescriptions of antipsychotic, anxiolytic, and mood stabilizing agents were compared between the two groups.
Results: Patients with borderline personality disorder were more likely to receive prescriptions for antipsychotic medication (OR=2.64, CI95=1.32-5.30, Wald X2=7.4, P=0.006) and mood stabilizing medication (OR=2.67, CI95=1.23-5.81, Wald X2=6.51, P=0.031). Quetiapine was more frequently prescribed (OR=2.97, CI95=1.21–7.30, Wald X2=5.63, P=0.018), as was divalproex sodium (OR=9.50, CI95=1.21–7.30, CI95=1.19–75.84, Wald X2= 4.53, P=0.034). There were no differences in the rates of prescriptions for lithium, other mood stabilizers, and other antipsychotics.
Conclusions: During this period of study, quetiapine and divalproex were favored medications for symptomatic treatment of patients hospitalized with borderline personality disorder.
NR269  Monday, May 3, 3:00 p.m.-5:00 p.m.
Olanzapine Plus Dialectical Behavior Therapy of Patients With BPD
Supported by Eli Lilly and Company

Joaquim Soler, Judith Barrachina, Josefa Campins, Dolores Puigdemont, Ph.D., Enrique Alvarez, M.D., Victor Perez, Ph.D.

Summary:
Objective: The aim of this study is to determine the efficacy and safety of olanzapine plus Dialectical Behavior Therapy (OLZ+DBT) versus placebo plus Dialectical Behavior Therapy (PLB+DBT) in the treatment of borderline personality disorder (BPD).

Method: A total of 60 BPD patients diagnosed by means of semi-structured interviews SCID-II and DIB-R were included in an uncenteric, double-blind, placebo-controlled study. Subjects were randomly assigned to olanzapine or placebo in a 1:1 ratio after a month baseline period. The length of the study was 15 weeks and all subjects received DBT. Measures included scales and self-reports related to affective, behavioral, psychosis and general psychopathology domains. This report presents data from clinical measures of safety and treatment response.

Results: The 70% of the patients completed the entire four-month trial. With a combined treatment we obtained an overall improvement in both groups in the majority of symptoms studied. Olanzapine was associated with a statistically significant improvement over placebo in depressive, anxiety and impulsivity symptoms. The olanzapine was a safe treatment, no serious side effects were observed.

Conclusions: Olanzapine appears to be an effective and safe treatment of BPD patients, significantly improve affect and impulsivity.

References:

NR270  Monday, May 3, 3:00 p.m.-5:00 p.m.
Temperament Dimensions in BPD: Evidence of Two Profiles

Johanne Maranda, M.P.S., Clinic le Faubourg, 175 Rue St. Jean, Quebec, QC G1R 1N4, Canada; Sandra Guimond, M.P.S., Sophie Lemelin, Ph.D., Sebastien Bouchard, M.P.S., Evens Villeneuve, M.D.

Educational Objectives:
At the conclusion of this session, the participant should acquire a better understanding of clinical symptom's heterogeneity among BPD evidenced by temperamental differences.

References:

NR271  Monday, May 3, 3:00 p.m.-5:00 p.m.
The Clinical Global-Impression Scale for Borderline Personality
Supported by Eli Lilly and Co.

Michael P. Bogenschutz, M.D., Psychiatry Department, University of New Mexico, 2400 Tucker NE, Albuquerque, NM 87131; Paula L. Hensley, M.D., Cynthia Geppert, M.D., Susan Paine, M.S., H. George Nurnberg, M.D.

Educational Objectives:
At the conclusion of this session, the participant should become familiar with the psychometric properties of a new instrument for measuring Borderline Personality Disorder symptomatology.

Summary:
Objective: Here we report preliminary psychometric data for the Clinical Global Impression for Borderline Personality Disorder (CGI-BPD), a new instrument to quantify BPD symptomatology.

Method: The CGI-BPD is a nine-item instrument consisting of the DSM-IV BPD criteria, each scored as 1–7 on a Likert scale, with anchors analogous to those of the clinical Global Impression (CGI). It served as the primary outcome measure in a pharmacotherapy trial including 40 female and male BPD patients. Internal consistency of the CGI-BPD was computed at each time point, and correlations with other outcome measures were computed at randomization and endpoint.

Results: Cronbach's alpha for the CGI-BPD ranged from .66 to .83 at the various time points. The scale was highly correlated with the single-item CGI at all time points. It was significantly correlated with total scores on the Overt Aggression Scale-Modified, the Anger, Irritability, and Assault Questionnaire, and the Symptom Checklist 90 at randomization and at endpoint. In addi-
tion to good reliability and concurrent validity, the CGI-BPD discriminated between patients treated with olanzapine and placebo. Conclusions: These preliminary data suggest that the CGI-BPD is a useful instrument for assessing BPD symptomatology. Further validation is needed.

Source of Funding: Eli Lilly and Co.

References:

NR272 Monday, May 3, 3:00 p.m.-05:00 p.m.
**BPD: Symptom Improvement With Quetiapine Supported by AstraZeneca Pharmaceuticals**

Evens Villeneuve, M.D., Lim le Faubourg, 175 Rue St. Jean, Quebec, QC G1R 1N4, Canada; Sophie Lemelin, Ph.D.

**Educational Objectives:**
At the conclusion of this session, the participant should be able to: (1) examine the efficacy and tolerability of quetiapine treatment in borderline personality disorder; (2) describe the improvement in symptoms and attentiveness of patients with borderline personality disorder treated with quetiapine.

**Summary:**
**Objective:** Affective, impulsive and interpersonal problems are the main symptom domains of borderline personality disorder (BPD). Studies in patients with schizophrenia suggest that quetiapine may improve a broad range of symptoms, including attention, also characteristic of patients with BPD (7).

**Method:** Twenty-three outpatients with BPD (DSM-IV criteria: DIB-R ≥ 7) [18–65 years] completed a 12-week, open-label, non-Comparative study to evaluate twice-daily quetiapine. The clinical efficacy of quetiapine on BPD symptomatology was evaluated using: HAM-D, HAM-A, Beck Hopelessness Scale, Brief Psychiatric Rating Scale (BPRS), Barratt Impulsivity Rating Scale, Buss-Durkey Hostility Inventory, Temperament and Character Inventory, and Global Assessment of Functioning. Attentiveness was examined using a computerized battery. Paired t-tests were performed and p values adjusted using a Bonferroni procedure.

**Results:** Mean daily dose of quetiapine 251 ± 50 mg (range 175-400 mg) was well tolerated. Depression and anxiety symptoms (p<0.0001), impulsivity (p<0.0001), hostility (p<0.0001), character dimensions (p<0.0001), and GAF scores (p<0.0001) were significantly reduced. There were non-significant reductions in the psychotic components of the BPRS, since patients did not present with psychotic symptoms. Selective attention (Stroop test) and divided attention (Dual task) both demonstrated significant improvements (p<0.05).

**Conclusion:** Quetiapine is effective in improving many characteristic symptoms of BPD

References:
2. Goldstein IM: Quetiapine reduces hostility and aggression with acute schizophrenia. 25th National Conference on Correctional Health Care, New Mexico, 2001

NR273 Monday, May 3, 3:00 p.m.-05:00 p.m.
**Relationship Between Defense Mechanism and Personality Disorders**

María E. Lopez-Ramirez, M.D., Psychology Department, Universidad Anahuac, Av. Lomas Anahuac Sin Numero, Mexico City 52786, Mexico; Enrique Chavez-Leon, M.D.

**Educational Objectives:**
At the conclusion of this session, the participant should be able to recognize the role of defense mechanisms in personality disorders and their importance to psychodynamic supportive psychotherapy.

**Summary:**
Personality disorders had called attention from psychiatrists and clinical psychologists because of their dysfunctional effect in interpersonal relations and their incapacity for adaptation in diverse situations. Some authors had stressed the important role of defense mechanisms in the success of psychotherapy for personality disorders.

**Objective:** The aim of this study was to evaluate the relationship between defense mechanisms and personality disorders in Mexican university students, to determine the relevance of this theme to psychodynamic supportive psychotherapy.

**Method:** To prove this, 241 subjects answered two questionnaires in the same session. DSQ-40 evaluates 20 defense mechanisms; PDQ-4+ evaluates 12 personality disorders.

**Results:** This study demonstrates that subjects with personality disorders use more immature and neurotic defense mechanisms. Factorial analysis of the PDQ-4+ revealed the presence of several dimensions that underline personality. For Cluster A we found: (1) a tendency to look for hidden meanings and to have extrasensory experiences; (2) the tendency to experiment anxiety in interpersonal relations; and (3) a drift to doubt constantly from others and to fear damage. For Cluster B, we found: (1) identity disturbances and emotional unsteadiness; (2) tendency to seek risk behaviors; and (3) necessity for calling attention. In Cluster C we found: (1) excessive necessity for support; (2) low self-esteem and self-criticism; and (3) rigidity and perfectionism.

References:

NR274 Monday, May 3, 3:00 p.m.-05:00 p.m.
**Topiramate as an Agent for Smoking Cessation?**

Nassima Alt-Daoud, M.D., Department of Psychiatry, University of Texas Health Science Center, 7703 Floyd Curl Drive, San Antonio, TX 78229; Bankole A. Johnson, M.D., Jennie Z. Ma, Ph.D., Fatema Z. Akhtar, M.S., John D. Roache, Ph.D., Norman Rosenthal, M.D., Charles L. Bowden, M.D., Carlo C. DiClemente, Ph.D., Martin A. Javors, Ph.D.

**Educational Objectives:**
At the conclusion of this session, the participant should have acquired (1) new knowledge on the comorbidity of alcohol and nicotine dependence, (2) knowledge on recent advances in the use of anticonvulsants to treat comorbid alcohol and nicotine dependence, and (3) new knowledge on the dual treatment of comorbid disorders.

**Summary:**
Introduction: Topiramate, a sulfamate fructo-pyranose derivative, may antagonize drug (including alcohol) reward associated...
with abuse liability by inhibiting mesocorticolimbic dopamine release, presumably via facilitation of gamma-amino-butyric acid activity and suppression of glutamate function. Consistent with this hypothesis, topiramate up to 300 mg/day, compared with placebo, significantly reduces drinking and craving in alcohol-dependent outpatients. Cigarette smoking, the leading cause of preventable death in the United States, is implicated in one of every five deaths. Over 80% of alcohol-dependent individuals also abuse or are dependent on nicotine. We, therefore, investigated whether topiramate would be effective at promoting smoking cessation.

Methods: In a randomized clinical trial of 150 individuals receiving topiramate (up to 300 mg/day) or placebo for the treatment of alcohol dependence, we assessed nicotine use during the medication treatment period of the study; 26 were smokers at baseline. Data analysis was adjusted for baseline characteristics including age, gender, body mass index, and past 90 days' nicotine use.

Results: Participants receiving topiramate, compared with placebo, were significantly more likely to become abstinent from nicotine (odds ratio = 2.5, 95% CI 1.01 – 6.38, p = 0.049).

Conclusion: These results provide evidence that topiramate may be a promising agent for the treatment of those co-dependent on nicotine and alcohol.

References:

NR275 Monday, May 3, 3:00 p.m.–05:00 p.m. Topiramate Treatment of Alcohol Dependence: Effects on Psychosocial Functioning and Its Relationship With Heavy Drinking

Bankole A. Johnson, M.D., Department of Psychiatry, University of Texas Health Science Center, 7703 Floyd Curl Drive, MS 7793, San Antonio, TX 78229-3900; Nassima Ait-Daoud, M.D., Jennie Z. Ma, Ph.D., Fatema Z. Akhtar, M.S., John D. Roache, Ph.D., Norman Rosenthal, M.D., Charles L. Bowden, M.D., Carlo C. DiClemente, Ph.D., Martin A. Javors, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should have acquired: (1) knowledge on recent scientific advances with a unique anticonvulsant, topiramate, for improving drinking and psychosocial outcomes in alcohol-dependent individuals; (2) new knowledge on the use of various anticonvulsants in the treatment of alcoholism; and (3) an understanding of the relationship between the treatment response to medication and psychosocial functioning.

Summary:
Introduction: Topiramate, a sulfamate fructose-pyranoside derivative, may antagonize alcohol reward associated with abuse liability by inhibiting mesocorticolimbic dopamine release, presumably via facilitation of gamma-amino-butyric acid activity and suppression of glutamate function. Consistent with this hypothesis, topiramate up to 300 mg/day, compared with placebo, significantly reduces heavy drinking among alcohol-dependent individuals. Nevertheless, does topiramate’s efficacy at improving drinking outcomes result in an appreciable improvement in psychosocial well-being or quality of life?

Methods: In a randomized, 12-week clinical trial of 150 individuals receiving topiramate (up to 300 mg/day) or placebo for the treatment of alcohol dependence, we assessed their quality of life and psychosocial functioning in addition to their drinking behavior.

Results: Topiramate was superior to placebo at improving the odds of overall well-being (odds ratio = 2.17, 95% CI 1.16–2.60, p = 0.0077) and overall life satisfaction (odds ratio = 2.28, 95% CI 1.21–4.29, p = 0.01). Reductions in heavy drinking were significantly correlated with improvements in quality of life and psychosocial functioning.

Conclusion: These results show that the topiramate-induced improvement in drinking outcome is sufficient to also enhance quality of life and psychosocial functioning among alcohol-dependent individuals. Our data continue to demonstrate topiramate’s utility in the treatment of alcohol dependence.

References:
Characteristic Differences Between Inhalant-Use and Heroin-Use Disorders

Cuneyt Evren, M.D., Amatem, Baktrkoy Mental Hospital, Icadlye Cad Mentes Sok 1/17, Uskudar Istanbul, Turkey, Omer Saatbioglu, M.D., Bilge Evren, M.D., Duran Cakmak, M.D.

Educational Objectives:
At the conclusion of this research, we should be able to demonstrate characteristics of inpatients with inhalant and heroin use disorders. Therefore, this is important for treatment strategies.

Summary:
Objective: Aim of this study was to compare sociodemographic and drug use characteristics between inhalant and heroin use disorder.

Method: The study was conducted between January 1998 and December 2002 in Bakirkoy State Hospital for Psychiatric and Neurological Diseases, AMATEM (Alcohol and Drug Research, Treatment and Education Center). Semistructured sociodemographic form have been applied to 539 patients with inhalant use disorder (IUD) and 841 patients with heroin use disorder (HUD).

Results: Female percentage was 2.8% for patients with IUD and 9.5% for patients with HUD. The mean age of the inhalant users was (23.81 ± 3.96) lower than the mean age of heroin users (34.03 ± 9.43). Among patients with IUD, percentage of being single, living with parents, alcohol dependence in family, dangerous and harmful behaviors while intoxicated and suicide attempt history was higher than patients with HUD. Among patients with HUD percentage of high school and university degree education, having substance related legal problems, imprisonment history, remission without treatment and previous hospitalization were high. Age of first substance use and age of heavy substance use was lower in patients with IUD. Inhalant was the first substance used by 80.7% of patients with IUD. Cannabis (58.9%) and heroin (25.4%) was the first substances used by patients with HUD.

Conclusion: Both patient groups with inhalant and heroin use disorder have the highest inpatient ratios than patients with other substances use disorder in Turkey. This two group differ from each other in terms of sociodemographic and drug use characteristics. Results suggest that differences should be taken in to consideration before planning treatment. Future research is needed to evaluate the effects of these differences on the course of the substance use disorder.

References:
Saiz, Ph.D., Begona Paredes, M.D., Jesus Delgado, Ph.D., Teresa Bascaran, M.D., Sara Martinez, Ph.D., Julio B. Bobes, M.D.

**Summary:**

**Objectives:** To describe the prevalence of cannabis consumption and the toxicological and psychological profile of a sample of military recruits.

**Subjects and Method:** WHO Drug Consumption Questionnaire, EPQ-A, Zuckerman Sensation Seeking Scale were administered to 3,634 conscripts [mean age (SD)= 20.19 (2.52)] who entered military service between 1995-99.

**Results:** Prevalence of cannabis use: lifetime: 40.0%, previous year: 25.9%, previous month: 17.3%. Cannabis ranking first among the illicit drugs ever used. When individuals used cannabis for the first time, they were likely to use it again (65% of individuals who had ever used cannabis had used it in the past year, 43.0% the last month). Mean age first use of cannabis was 16.04 (2.23). Polysubstance usage and cannabis use was (98.1%), tobacco (95.3%), hallucinogens (32.5%), and amphetamines (29.3%). Recruits who had ever used cannabis had significantly higher scores on the EPQ-A and reported higher levels of sensation seeking (p=.000).

**Conclusions:** Cannabis users are polyconsumers of other drugs. Cannabis users have a different psychological profile characterized by higher levels of emotional instability, extraversion, and psychoticism, as well as a marked sensation seeking profile.

**References:**


**NR280**

**Monday, May 3, 3:00 p.m.-5:00 p.m.**

**Personality Disorders, Quality of Life, and Addiction Treatment**

Juan J. Fernandez-Miranda, M.D., Psychiatry Department, Oviedo University, Julian Claveria 6-3, Oviedo 33006, Spain; Maria P. G-Portilla, Ph.D., Pilar A. Saiz, Ph.D., Eduardo Gutierrez, M.D., Julio B. Bobes, M.D.

**Summary:**

In order to determine the prevalence of personality disorders (PD) in a population undergoing methadone maintenance treatment and how they influence treatment outcomes, including quality of life, 50 patients were followed up over a six-year period of treatment. The A.S.I., I.P.D.E., and SF-36 were administered.

MMT proved to be highly effective, leading to decreased drug use (e.g. 100% to 12% heroin use, 34% to 12% cocaine use) and improved social (less legal problems an higher employment rates) and medical status, and also quality of life. PD were found in half of all subjects studied. The most common PD were antisocial (26.5%) and borderline (18.1%). Given that PD were found in a population with low addiction severity after six years in MMT, we considered that these PD were not the result of current dependant-behavior. Though patients with PD had clearly improved their situation since entering the MMT, they tended to achieve poorer treatment outcomes (higher use of cocaine and tranquillizers, lower family and employment improvement, worse psychological status; p<.05) and quality of life (in physically, vitality and mental health domains; p<.05). If MMT programs are to be more effective, greater attention must be paid to diagnosing and specifically treating PD.

**References:**


2. Kranzler HR, Burleson JA, Brown J, Babor TF. Fluoxetine treatment seems to reduce the beneficial effects of cognitive-behav-
NR282  Monday, May 3, 3:00 p.m.-5:00 p.m.
Cognitive Function of Detoxified and Methadone-Maintained Opiate Abusers

Matthew Steinfeld, B.A., Department of Psychiatry, Beth Israel Medical Center, 1st Avenue and 16th Street-6Karpas, New York, NY 10003; Enid C. Gertmenian-King, B.A., Lisa J. Cohen, Ph.D., Igor I. Galynker, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the relationship between methadone treatment and cognitive function in opiate abusers.

Summary:
Background: Cognitive impairment in opiate abusers may contribute to non-compliance with treatment and therefore to perpetuation of addictive behaviors. The effects of methadone maintenance and methadone detoxification on the neurocognitive functioning of opiate addicts are poorly understood.

Methods: In the present study, we have compared a rigorously selected sample of 29 methadone-maintained (MM) and 27 methadone withdrawn (MW) abstinence addicts in relation to 29 healthy control subjects on a battery of neuropsychological tests.

Results: The three groups differed on the WAIS-R vocabulary test (F(3,62)= 21.85, p<.001), the Stroop Interference task (F(3,62)= 3.35, p=0.021), total errors (F(3,62)= 8.66, p=.001), right-sided errors (F(3,62)= 8.66, p<.001), left-sided errors (F(3,62)=4.43, p=.007), and total correct (F(3,62)=8.45, p<.001) on the Benton Visual Retention Test. By pairwise comparisons, MW subjects scored worse than controls on five tests, MM scored worse than controls on one test, and MW subjects scored worse than MM subjects did on one test.

Conclusion: Both MM and MW groups showed significant impairment relative to controls, suggesting severe neurocognitive sequelae of chronic opiate abuse. However, the MW group scored slightly worse than MM patients, which may reflect either an extended withdrawal effect or beneficial effects of methadone maintenance treatment.

Funding Source(s): NIDA #R01DA12272-01 awarded to Dr. Galynker

References:

NR283  Monday, May 3, 3:00 p.m.-5:00 p.m.
Divided Attention and Pain Processing in Opiate Abusers

Matthew Steinfeld, B.A., Department of Psychiatry, Beth Israel Medical Center, 1st Avenue and 16th Street-6Karpas, New York, NY 10003; Lauren Kunik, Enid C. Gertmenian-King, B.A., William H. Gottdinner, Ph.D., Lisa J. Cohen, Ph.D., Igor I. Galynker, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the relationship between pain processing and attentional performance in opiate addicts.

Summary:
Objective: Methadone maintenance is the primary treatment for opiate addiction, but controversy surrounds the merits of long-term methadone treatment. This study tested whether methadone-withdrawn opiate addicts have abnormalities in the neural circuitry that mediates dysphoric emotion, and whether such problems are less evident in opiate addicts on methadone maintenance therapy.

Method: Fifteen abstinent opiate addicts free of methadone (6–24 months), and twelve abstinent opiate addicts on methadone maintenance were compared on measures of dysphoric emotion and relative rCMRglc with thirteen control subjects.

Results: SPM-99 analysis revealed that methadone-withdrawn opiate addicts had lower relative activity than controls in the infragenual and perigenual anterior cingulate gyrus (ACG) and the left midcingulate cortex. Methadone-maintained subjects similarly exhibited lower relative activity in the midcingulate cortex as well.

Summary:
Background: Detoxified opiate abusers demonstrated functional impairment in regions of the Anterior Cingulate Gyrus, which mediates divided attention and the emotional aspects of pain. The purpose of this ongoing study is to assess the experience of pain, divided attention, and the interaction between the two in opiate abusers.

Method: The TSA-II NeuroSensory Analyzer, a computerized, quantitative thermal sensory testing device, was used to assess pain threshold. Performance on the Stroop CW test during painful vs. non-painful conditions was compared across three subject groups; 11 methadone-withdrawn, abstinent opiate addicts (MW), eight methadone-maintained (MM), and 11 healthy controls.

Results: The difference in Stroop performance during painful vs. non-painful conditions varied significantly across groups (F(2,30)= 3.428, p=.047). While MW showed a significant improvement under painful stimuli (t(11)= -3.282, p=.007), Controls showed a slight, non-significant improvement and MM showed no change in performance under painful stimuli. The three groups did not differ significantly on pain threshold or subjective measures of pain.

Conclusion: Detoxified opiate abusers may have aberrant interaction between pain processing and divided attention, which is normalized by methadone maintenance.

Funding Source(s): Rothschild Foundation, 2002, awarded to Dr. Galynker

References:

NR284  Monday, May 3, 3:00 p.m.-5:00 p.m.
Dysphoric Emotion and rCMRglc in Opiate Abusers Receiving or Removed From MMT

Igor I. Galynker, M.D., Department of Psychiatry, Beth Israel Medical Center, First Avenue at 16th Street, Room 6K42, New York, NY 10003; Enid C. Gertmenian-King, B.A., John A. Matochik, Ph.D., Lisa J. Cohen, Ph.D., Alane S. Kimes, Ph.D., Carlo Contoreggi, M.D., Eddythe London, Ph.D.

Educational Objectives:
At the conclusion of the session, participants should appreciate that opiate exhibit abnormalities in the neural circuitry subserving dysphoric emotion which are partially ameliorated by methadone maintenance.

Summary:
Objective: Methadone maintenance is the primary treatment for opiate addiction, but controversy surrounds the merits of long-term methadone treatment. This study tested whether methadone-withdrawn opiate abusers have abnormalities in the neural circuitry that mediates dysphoric emotion, and whether such problems are less evident in opiate abusers on methadone maintenance therapy.

Method: Fifteen abstinent opiate abusers free of methadone (6–24 months), and twelve abstinent opiate addicts on methadone maintenance were compared on measures of dysphoric emotion and relative rCMRglc with thirteen control subjects.

Results: SPM-99 analysis revealed that methadone-withdrawn opiate abusers had lower relative activity than controls in the infragenual and perigenual anterior cingulate gyrus (ACG) and the left midcingulate cortex. Methadone-maintained subjects similarly exhibited lower relative activity in the midcingulate cortex as well.
as in the insula, thalamus, and left inferior parietal lobule; they exceeded control activity in the perigenual ACG and right inferior parietal lobule. Methadone-withdrawn subjects showed positive correlations between measures of depression and rCMRglc in the mid-cingulate cortex and in left perigenual ACG: analogous associations in control and methadone-maintained subjects were mostly negative.

Conclusions: Opiate abusers exhibit abnormalities in the neural circuitry subserving dysphoric emotion which are partially ameliorated by methadone maintenance.

Funding Source(s): NIDA #R01DA12273-01 awarded to Dr. Galynker

References:
2. Condelli W.S., Dunteman G.H. Exposure to Methadone Pro-

NR286  Monday, May 3, 3:00 p.m.-5:00 p.m.
Personality Profiles Across Addictive Behaviors
Yuli Grebchenko, M.D., Department of Psychiatry, Beth Israel Medical Center, 1st Avenue and 16th Street 6K42, New York, NY 10003; Alisa Turok, M.D., Matthew Steinfeld, B.A., Lauren Kunik, Soenke Boettger, M.D., Igor I. Galynker, M.D., Lisa J. Cohen, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the patterns of personality impairment in two groups of addictive behaviors.

Summary:
Background: The purpose of this ongoing study was to compare the personality profiles of 2 groups of impulsive, addictive, sociopathic patients in order to determine if there is a specific pattern of personality impairment in pedophiles. Such findings could contribute to advances in the treatment and prevention of pedophilia.

Methods: A rigorously selected sample of 13 pedophiles (PEDs) and 15 abstinent and methadone-withdrawn, opiate addicts (OAs) were compared in relation to nine healthy control subjects on the Structured Clinical Interview for DSM-IV (SCID II) and the Hare Psychopathy Checklist Revised (PCL-R).

Results: Pedophiles, Opiate abusers and normal controls were compared by 3 group ANOVA’s with follow-up Scheffe paired comparisons. The three groups differed on number of Cluster A traits (F(2,40)=6.82, p=.003), and marginally differed on Cluster C traits (F(2,40)=2.46, p=.099) and on Factor 1 of the PCL-R (F(2,36)=3.17, p=.055). Both pedophiles and opiate addicts showed more impairment than controls on Cluster A personality traits and PEDs had marginally higher scores on Factor 1 of the PCL-R. The three groups also differed on paranoid (F(2,40)=5.72, p=0.007) and schizoid personality traits (F(2,40)=7.08, p=0.002) with both PED and OA groups scoring higher than controls in both cases.

Conclusion: Both PED and OA groups showed similar patterns of personality impairment relative to controls. Although we could not identify a personality profile specific to pedophiles, there may be a personality profile common to different impulsive, addictive, sociopathic groups.

References:

NR285  Monday, May 3, 3:00 p.m.-5:00 p.m.
Time Since Detoxification and rCMRglc Abnormalities in Opiate Abusers
Igor I. Ga

Educational Objectives:
At the conclusion of the session, participants should understand that Relative MMRglc in detoxified opiate abusers varies with increased interval from detoxification but not necessarily in the direction of that in healthy controls.

Summary:
Objective: The relationship between duration of opiate abstinence and relative rCMRglc in detoxified opiate abusers may be of importance in understanding their vulnerability to relapse. This study tested whether methadone-withdrawn opiate abusers who are more recently detoxified have different abnormalities in the neural circuitry that mediates dysphoric emotion than those with greater time since detoxification.

Method: Nine opiate abusers detoxified from methadone for 6–8 months (6M) and 24 months (10M) and thirteen control (C) subjects.

Results: Subjects in both 6M and 10M groups had lower relative activity than controls in the bilateral perigenual anterior cingulate gyrus and in left midcingulate cortex. 6M subjects also exhibited lower relative activity in the superior frontal gyrus bilaterally. Activity in the right inferior parietal lobule of 10M subjects exceeded that of both 6M subjects and controls. As a whole, methadone-withdrawn subjects showed a positive correlation between time since detoxification and relative rCMRglc in the right inferior parietal cortex, and a negative correlation between the same variables in the bilateral superior frontal gyrus.

Conclusions: Relative rCMRglc in detoxified opiate abusers varies with increased interval from detoxification but not necessarily in the direction of that in healthy controls.

Funding Source(s): NIDA #R01DA12273-01 awarded to Dr. Galynker

References:
Objective: Methamphetamine (MA) dependence accounts for substantial morbidity in veterans. We hypothesized that chronic MA abusers would be impaired relative to non-addicts on measures of psychopathology, neuropsychological function and impulsivity.

Methods: Forty-one currently abstinent MA abusers and 41 age, gender and education matched controls gave informed consent. Patients met DSM-IV criteria for MA dependence, had average daily use of 0.5 g/da (0.5 to 6 g/da), had been abstinent at least two weeks (2-24 wk) and had a negative urine drug screen within one week of evaluation. Psychiatric symptoms were rated on standardized scales. Neuropsychological function was assessed with a battery of standardized tests. Impulsivity was assessed using Delay Discounting, a procedure that asks subjects to evaluate delayed versus immediate rewards.

Results: Patients reported more psychiatric symptoms than controls on each subscale (Positive, Negative, General) of the Positive and Negative Syndrome Scale (PANSS) (p < .001). MA addicts were significantly more likely to prefer immediate vs. delayed rewards.

Conclusion: Chronic methamphetamine abuse is associated with increased psychiatric morbidity, memory deficits and impulsivity.

Implications for Future Research: Cognitive impairment and impulsivity in chronic MA abusers may either result from abuse or be a pre-existing risk factor. Studies under way will investigate recovery from methamphetamine abuse and use functional neuroimaging to establish the neural bases for these deficits.

References:

NR288 Monday, May 3, 3:00 p.m.-5:00 p.m.
Substance Use Disorders in First-Degree Relatives of Opioid-Dependent Males
Debasish Basu, M.D., PGMER, Chandigarh, UT 160012, India; Mulakaluri P, Prasanath, M.D., Surendra K. Mattoo, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to appreciate family history issues in opioid dependence.

Summary:
Aim: To assess the prevalence of psychiatric disorders, including substance use disorders, in first-degree relatives (FDRs) of probands with opioid dependence.

Design: A case-control design.

Methods: Lifetime prevalence of psychiatric disorders in 493 FDRs of 100 male probands compared with those in 254 FDRs of 50 normal controls.

Measurements: Morbid risk (Weinberg’s) and relative risk (adjustable OR using logistic regression).

Findings: Overall, FDRs of opioid probands had 4.12-times higher risk for familial aggregation of any psychiatric disorder compared to normal controls (p < .001). The elevated risk for alcohol dependence was mostly observed in the fathers of the probands (adj. OR = 5.6; P < 0.001). The morbid risk for opioid dependence in FDRs was 4.3%, accounted for mostly by the brothers of the probands (adj. OR = 6.5; P = 0.015).

Conclusion: The role of gender and type of relation of the FDRs emerged as an important factor in defining the familial risk of dependence on alcohol vs. opioids in this sample. An interaction of genetic and cultural factors is suggested.

References:
**NR290**  
Monday, May 3, 3:00 p.m.—5:00 p.m.  
Self-Reported Reasons for Cannabis Use Among Recovering Substance Abusers  
Joao E. Marques-Teixeira, Ph.D., Hosp. Conde Ferreiruesm; R Costa Cabral 1211, Porto 4200-227, Portugal; Rosa Goncalves, M.D., Filipa Palha, Psy.D.  

**Educational Objectives:**  
At the conclusion of this poster session, the participant should be able to recognize the necessity of developing medical and psychological strategies in order to improve stress relief following heroine detoxification.  

**Summary:**  
Objective: To examine prevalence, coping, self-concept, and self-reported attributions for cannabis use among individuals undergoing an addiction treatment program for heroine-addicts.  

Method: Sixty-nine long-term drug abusers (mean age = 35.9, sd = 6.25) undergoing an addiction treatment program completed Self-Concept Clinical Inventory (Vaz-Serra, 1986) and Ways of Coping Questionnaire (Folkman & Lazarus, 1985). Cannabis use and self-attributions to it were assessed through a structured interview. Analysis was carried out in four groups of different cannabis use patterns (maintaining, increasing, decreasing and never used).  

Results: We found no significant differences between using vs never used cannabis groups on demographic variables, and on self-concept. Sixteen percent of the subjects maintained, 41% increased, 26% diminished, and 17% never used cannabis. The majority of subjects show non organized coping strategies. Subjective attributions to cannabis use show that the increasing use subjects reported 36% of their answers to self-medication, while the decreasing use subjects reported 20% of their answers to recreational use and 20% to negative effects.  

Conclusion: A great percentage of heroine drug-addicts increase cannabis use after their heroin detoxification, attributing their use to self-medication. Thus, it seems important to develop pharmacological and psychological strategies in order to improve stress relief.  

**References:**  

**NR291**  
Monday, May 3, 3:00 p.m.—5:00 p.m.  
Depression and Access to Hepatitis-C Treatment in Methadone Patients  
Arjun K. Srinath, Psychiatry Department, SUNY Upstate Medical University, 750 East Adams Street, Syracuse, NY 13210; Steven L. Batki, M.D., Martha Cornell, R.N., Michelle Bowman, Roos Peek, Michael Wade, M.S., Jacqueline Dimmock, Ph.D., Myrurgia Abdul-Hamid  

**Educational Objectives:**  
At the conclusion of this session, the participant should recognize the frequent occurrence of depression among methadone patients with Hepatitis C infection and its relationship to access to Hepatitis C treatment.

**Summary:**  
Objective: To examine psychiatric factors affecting Hepatitis C (HCV) treatment access among methadone maintenance treatment (MMT) patients.  

Method: Interviews were conducted with 82 HCV + MMT patients.  

Results: Mean age was 41.6; 51 patients (62%) were male and 51 (62%) were Caucasian. Seventy (85.4%) had health insurance and 12 (14.6%) were uninsured. Thirty-five (42.7%) had a Beck Depression (BDI) score greater than 15. Those offered HCV treatment did not have significantly different rates of depression or different mean BDI scores than those not offered treatment. Of patients offered HCV treatment, 86% of those who had never been treated for depression actually started HCV treatment, while only 58% of those ever treated for depression started HCV treatment; however, this difference was not statistically significant.  

Conclusion: Most HCV + MMT patients reported having a mental health problem, most commonly depression. While depression affected the majority of patients, it did not appear to be significantly associated with reduced access to HCV care in this sample.  

**References:**  

**NR292**  
Monday, May 3, 3:00 p.m.—5:00 p.m.  
Relationship of Serotonin Transporter Polymorphism to Treatment Outcome in Cocaine Dependence  
Marja Mattila-Evenden, M.D., Psychiatry Department, Thomas Jefferson University, 833 Chestnut Street, Suite 210E, Philadelphia, PA 19107; Ashwin A. Patkar, M.D., Paolo Mannelli, M.D., Kathleen S. Peindl, Ph.D., Heather W. Murray, M.S., Louai A. Bilal, M.D., Wade H. Berrettini, M.D.  

**Educational Objectives:**  
At the conclusion of this session, the participant should recognize the influence of genetic factors in treatment outcome in Substance Abuse.  

**Summary:**  
Introduction: Brain serotonin transmission, and the serotonin transporter in particular, may play an important role in modulating effects of cocaine. A polymorphism in the promoter region of the serotonin transporter gene (5-HTTLPR) has been associated with differences in the expression of alcohol and cocaine abuse. We investigated whether 5-HTTLPR variants were related to different measures of treatment outcome in cocaine dependence.  

Methods: Polymerase chain reaction-based genotyping of a 44 base pair insertion/deletion polymorphism in 5-HTTLPR, yielding a short (S) and a long (L) allele, was performed in a sample of 141 severely cocaine dependent African American subjects entering a 12-week outpatient treatment program. Measures of abstinence and retention during treatment period and at 6 months follow-up were employed as outcome variables. Changes from ASI composite scores at admission were adopted as a measure of addiction severity at same time points.
Results: No significant relationship was observed between polymorphic variants of the 5HTTLPR region and demographic variables, or any of the outcome measures. In particular, the change in severity of substance use was not related with genotype distributions (p = 0.844) of the variants among cocaine dependent patients, although a significant treatment effect (p < 0.001) was observed in all three genotypes.

Conclusion: The findings do not seem to support an association between this polymorphism in the SHTT gene and measures of treatment outcome among cocaine dependent African American individuals.

Funding Source(s): National Institute on Drug Abuse

References:

NR293 Monday, May 3, 3:00 p.m.-5:00 p.m.
The Association Study of Dopamine Transporter Gene and Amphetamine Abuse
Jia-Fu Lee, Ph.D., Department of Psychiatry, Armed Forces PT H, No60 Hsin-Ming Road PEI-TOU District, Taipei, Taiwan; Chia-Chi Chen, M.S., Ming-Yung Lee, M.D., Kuo-Chuan Huang, M.D., Huan-Kwang Ferng, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the association between dopamine transporter gene and amphetamine abuse.

Summary:
The dopamine transporter (DAT) is the primary mechanism for dopamine clearance from the synapse in midbrain dopaminergic neurons, and the target of psychostimulant and neurotoxic drugs such as amphetamine. The gene for DAT (SLC6A3) has been the focus of many population-based case-control association studies using a 40-bp VNTR in the 3'-untranslated region. The dopamine transporter (DAT) plays a central role in dopaminergic neurotransmission in the human brain. Genetic association studies have used a variable number of tandem repeat (VNTR) polymorphism in the 3'-flanking region of the dopamine transporter gene (DAT1) to implicate the DAT in the development of various neuropsychiatric disorders and substance dependence disorder. In this study, we have examined this hypothesis and try to test the association between the 10-repeat VNTR DAT1 polymorphism and Amphetamine abuse in the samples of Taiwanese Han. There were 80 Amphetamine Abuse cases (according to DSM-IV) derived from Han male criminals. The 80 controls without any illegal substance misuse history were recruited from the community. All of the subjects are Taiwanese Han males. The results showed no significant differences were observed between the subject groups of amphetamine abuse and controls. These results exclude a major effect of the Dopamine Transporter polymorphism on Amphetamine abuse.

Funding Source(s): The research was supported by DOH-NNB-1007

References:

NR294 Monday, May 3, 3:00 p.m.-5:00 p.m.
Comorbid Psychiatric Diagnosis in Impulse Control Disorders: Kleptomania Versus Pathological Gambling
Pinhas N. Dannon, M.D., Community Clinic, Ness Ziona Medical Center, Remez St. 80, Rehovot 76449, Israel; Katherine Lowengrub, M.D., Moshe Kotler, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to explore the relationship between kleptomania, pathological gambling, depression, and anxiety.

Summary:
Kleptomania and pathological gambling are currently classified in the DSM-IV as disorders of impulse control. Impulse-control disorders are characterized by an overwhelming temptation to perform an act that is harmful to the person or others. The patient usually feels a sense of tension before committing the act and then experiences pleasure or relief while in the process of performing the act. Kleptomania and pathological gambling are often associated with other comorbid psychiatric diagnoses. Our study explored the relationship between kleptomania, pathological gambling, depression, and anxiety.

Forty-four pathological gamblers and 19 kleptomanics were included in this study. All enrolled patients underwent a complete diagnostic psychiatric evaluation and were examined for symptoms of depression and anxiety using the Hamilton Depression Rating Scale and the Hamilton Anxiety Rating Scale respectively. In addition, the patients completed self-report questionnaires about their demographic status. The study results demonstrated that pathological gambling is strongly correlated with affective disorders, suicidal behavior and substance abuse. The comorbid diagnoses found at a high prevalence among our kleptomanic patients included affective and anxiety disorders. A larger study is needed to confirm these preliminary results.

References:

NR295 Monday, May 3, 3:00 p.m.-5:00 p.m.
Is Pathological Gambling an Impulse Control Disorder or an Addiction? Israeli Male Pathological Gamblers Profile
Pinhas N. Dannon, M.D., Community Clinic, Ness Ziona Medical Center, Remez St. 80, Rehovot 76449, Israel; Katherine Lowengrub, M.D., Moshe Kotler, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to present our findings regarding the comorbid psychopathology among our cohort of PG patients.
Sustained-Release Bupropion Treatment of Pathological Gambling: A Pilot Study
Pinhas N. Dannon, M.D., Community Clinic, Ness Ziona Medical Center, Remez St. 80, Rehovot 76449, Israel; Katherine Lowengrub, M.D., Moshe Kotler, M.D.

Educational Objectives:
At the conclusion of this session, the participants should be able to show the effectiveness of bupropion sustained release (SR) in PG.

Summary:
Background: Pathological gambling (PG) is a highly prevalent and disabling impulse control disorder. Recently there have been studies which have consistently shown that PG patients have responded well to treatment with SSRI's, mood stabilizers, and opioid agonist/antagonists. These findings have supported the observation that PG is strongly associated with both mood and anxiety disorders. The aim of our study is to present our findings regarding the comorbid psychopathology among our cohort of PG patients.

Methods: Thirty-five male PGs were enrolled in our study. A comprehensive psychiatric diagnostic evaluation was performed on all patients, and patients were screened for symptoms of depression and anxiety using the Hamilton Depression Rating Scale, the Hamilton Anxiety Rating Scale, and the Frost Multidimensional Perfectionism Scale. In addition, the patients completed self-report questionnaires about their demographic status.

Results: The majority of patients were married with full- or part-time employment. The study results demonstrated that PG is strongly correlated with substance and alcohol abuse. Other diagnoses which were prevalent among our cohort of PGs included major depression, bipolar disorder, type I and type II, and anxiety disorders.

Conclusion: The high comorbidity for disorders of alcohol and substance abuse seen in our sample of PG patients suggests the possibility of a common underlying etiological mechanism.

References:

Effectiveness of Topiramate in the Control of Craving in Drug Dependence
Julio B. Bobes, M.D., Department of Psychiatry, University Oviedo, Julian Claveria 6, Oviedo 33006, Spain; Eduardo Carreno, M.D., Eduardo Gutierrez, M.D., Gemma San Narciso, Oviedo, Julian Claveria 6, Oviedo 33006, Spain; Eduardo Carreno, M.D., Eduardo Gutierrez, M.D., Gemma San Narciso.

Summary:
Introduction: Like in most industrialized countries, in Germany alcoholism is a major source for medical costs and productivity loss. Real economic impact is unknown, however.

Replicating similar US studies (Holder et al. 1999), we analyzed economic costs of alcohol dependent persons of a south-western branch of the major German health insurance company (AOK).

Method: We assessed annual costs of all inpatient treatments of AOK members who had at least one hospital stay due to alcoholism (ICD-9 303) in 1998. Sample size was n=227, mean age was 43 years, 88.5% were male, 92.4% of German nationality.

Results: Costs of all hospital stays (due to alcoholism or any other illness) of a study patient in 1998 came up to 11.149 $ in average, whereas annual inpatient treatment costs of all AOK members were only 3.534 $. Sick-pays and costs of work absences of study patients rose to an annual average of 16,224 $. Study patients were absent from work in 162 days in average. Thus, societal cost amounted to a total of 27,373 $.

Conclusions: Costs for alcohol dependent persons burden the national German economy to a high degree. Further studies are crucial for identifying cost-effective treatment strategies likely to reducing societal cost.

References:
M.D., M. Jesus Antuna, M.D., Tomas Diaz Gonzalez, M.D., Juan J. Fernandez-Miranda, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to know the improvement in craving after Topiramate add-on treatment.

Summary:

Introduction: Gabaergic, glutamatergic and serotonergic systems are implicated in the neurobiology of craving. The mechanism of action of topiramate may involve those systems. This preliminary study was aimed to evaluate the effectiveness of topiramate, as add-on treatment in craving management.

Material and Methods: An open, multi-center study was designed and 75 patients (79.3% male, mean age 28.8 ± 5.1 years) were included. Patients were diagnosed as having substance dependence, with an average duration of the consumption of five years. Systematic evaluation during a six-month follow-up was performed using regular urine screening, and the following scales in order to evaluate the craving for substances and mood changes: EuropASI, Philadelphia Craving Scale, Visual Analogic Scale (VAS) for Craving, and HAM-D.

Results: Fifty (66.7%) patients completed the study. Mean topiramate dose at the end of the study was 147 ± 71 mg/day. There was a significant reduction in the mean number of positive urine tests, between baseline and the end of the study (94.1% vs. 39.6%, p<0.001). A significant clinical improvement in all scales used was also observed.

Side effects were reported in 28% of the patients. The most frequent were somnolence (11%), paraesthesia (7.3%), and depression (4.9%). Two patients needed to be withdrawn due to side effects (one for amnesia and one for paraesthesia).

Conclusions: Despite the limitations this open study showed that addition of topiramate significantly reduced craving and consumption of substances. There were no major safety issues in our sample. Further research is needed.

References:

NR300 May 3, 3:00 p.m.-5:00 p.m.
Evaluation of Long-Term Abstinence After Rapid Opiate Detoxification Under General Anaesthesia
Emmanuel B. Pinto, M.D., Department of Psychiatry, Université de Liege, Ché Zart Tilmann B35, Liege 4000, Belgium; Jean Reggers, Ph.D., Sonia Fuchs, M.D., Ingrid Venneman, M.D., Maurice Lamy, M.D., Marc Ansseau, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to evaluate the usefulness of a RODA for opiate dependent patients.

Summary:

Objectives: Many studies support the hypothesis of a substantial benefit in inducing an Opiate Receptor Blockade through a Rapid Opiate Detoxification under general Anaesthesia (RODA) in opiate dependent patients. Our objective was to evaluate long-term abstinence rates after a RODA among a sample of opiate addicts, as well as patients’ characteristics that could be predictive of a better outcome.


Results: To date, 53 opiate dependent patients (aged 29 ± 5 years) with a mean opiate dependence of 10 ± 3 years have been screened. 27 (51%) were included. None experienced severe withdrawal symptoms. After six months abstinence rate was 63% and 46% after one year. 43% of the patients were still abstinent after 18 months. Patient on methadone maintenance programs seemed to do better than heroin or heroin-methadone users.

Conclusions: These preliminary results suggest the interest of the procedure in carefully selected patients. Further investigation should focus on the interest of switching heroin addicts to methadone prior to RODA.

References:

NR301 May 3, 3:00 p.m.-5:00 p.m.
Undiagnosed Bipolar Disorder in Patients With Substance-Use Disorder Supported by Abbott Laboratories
Mark J. Albanese, M.D., Department of Psychiatry, Cambridge Hospital, 26 Central Street, Somerville, MA 02143

Educational Objectives:

At the conclusion of this session, the participant should be able to: (1) better diagnose bipolar disorder in the presence of a substance use disorder; and (2) formulate a more appropriate treatment plan for bipolar patients with substance use disorder.

Summary:

Objective: Reports have been emerging that bipolar disorder is frequently undiagnosed or misdiagnosed. Patients with substance use disorders (SUD) are at increased risk of having a comorbid bipolar disorder. Because the co-occurrence of these disorders results in poorer course and outcomes, adequate identification and treatment of both disorders is crucial. This poster reports on undiagnosed bipolar disorder in a SUD population.

Method: Two hundred ninety-five patients admitted to a short-term post-detoxification residential substance abuse program were referred for psychiatric assessment. After a structured clinical interview, DSM-IV diagnoses were assigned. Eighty-five patients were diagnosed with bipolar disorder, and they are the focus of this report. All patients were Caucasian men, with a mean age of 32.3 years.

Results: (1) 42 of the 85 patients (49%) had not been diagnosed previously. (2) Six of the 42 patients had not been evaluated previously. (3) The remaining 36 had previously received a variety of other psychiatric diagnoses, mainly major depression (25; 69%). (4) 20 patients (57%) had been treated with an antidepressant alone.
Conclusions: This report suggests that many bipolar SUD patients go undiagnosed and, therefore, inadequately treated.

Funding Source(s): Abbott Janssen and the Arcadia Charitable Trust

References:


NR302 Monday, May 3, 3:00 p.m.-5:00 p.m.
Outpatient Treatment of Substance Abuse Withdrawal
Harold B. Pinkofsky, M.D., Department of Psychiatry, WPIC-CPCDS, 3501 Forbes Avenue, 9th Floor, Pittsburgh, PA 15213; Ann Hahn, R.N., Vineeth John, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to discuss the potential role for opioid treatment of substance abuse withdrawal.

Summary:
Objective: To determine the efficacy of outpatient treatment of detoxification/withdrawal in active substance abusers.

Methods: Patients attending an outpatient clinic for management of withdrawal symptoms in substance abusers were monitored for outcome rates. The efficacy of treatment protocol was measured by examination of program completion and treatment follow-up. The clinic's patient population included individuals withdrawing from opioid, alcohol and benzodiazepine abuse. Individuals were monitored on a daily basis for symptoms of withdrawal and vital signs.

Results: During a six-month period a total of 188 individuals were enrolled in the clinic, with a total of 516 visits. Of this cohort 52% successfully completed the program, finishing at least five days of abstinence. Of those completing the program 77% followed up by attending a daily aftercare program.

Conclusions: The results suggest a role for an outpatient clinic in treating withdrawal in substance abusers.

Funding Source(s): Quetiapine samples were provided by Astrazeneca.

References:


NR304 Monday, May 3, 3:00 p.m.-5:00 p.m.
Trichotillomania: Impact on Daily Functioning and Quality of Life
Gretchen Diefenbach, Ph.D., Anxiety Disorders Clinic, Institute of Living, 200 Retreat Avenue, Hartford, CT 06106; David Tolin, Ph.D., Scott Hannan, Ph.D., Johanna Crocetto, M.S., Patrick Worhunsky, B.S.

Educational Objectives:
At the conclusion of this session, the participant should be able to identify the ways in which hair pulling impacts quality of life.

Summary:
Objective: Although trichotillomania (TTM) was once considered benign, increasing research suggests that hair pulling can have a significant impact on patient's lives. The goal of the current study was to identify the impact of hair pulling on quality of life.

Methods: Patients with TTM (n = 20), patients with anxiety disorders (n = 22), and nonclinical control participants (n = 10) were compared on quality of life measures (QOLI; SAS-SR, and SDS). In addition, descriptive information regarding the impact of TTM on quality of life was collected.

Results: Analysis of variance indicated that the groups differed significantly on the QOLI, SDS-work scale, SDS-social scale, and SDS-family scale (all p < .004). Generally TTM patient reported impaired quality of life relative to control participants. In addition, data indicated 32% to 100% of TTM patients endorsed problems with functioning over a range of domains (grooming, physical health, social interaction, recreational activities, and work productivity). Data collection is ongoing, and data from the larger sample will be presented.
Conclusions: This study provides both descriptive and quantitative information about the impact of hair pulling on patient's daily lives, and underscores the importance of continued research efforts to improve care for TTM patients.

Funding Source(s): Hartford Hospital New Investigator's Grant # 126082

References:

NR305 Monday, May 3, 3:00 p.m.–5:00 p.m.
The Continuity of Maternal Depression in the First Three Years After Childbirth
Li-Ching Lee, Ph.D., Bloomberg School of Public Health, Johns Hopkins University, 615 N. Wolfe Street, Room E6516 Baltimore, MD 21205; Carolyn T. Halpern, Ph.D., Inva Hertz-Picciotto, Ph.D., Sandra L. Martin, Ph.D., Chirayath M. Suchindraw, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the patterns of depressive symptoms among childbearing women, and to understand that these patterns can be very different for women who have the same characteristics (e.g. race, age, education, employment, etc.)

Summary:
Objective: The purpose of this study was to examine the trend and patterns of maternal depressive symptoms during offspring’s first three years of life.
Method: Analyses were based on prospective longitudinal data from the Study of Early Child Care. Repeat-measured data were collected from 1,364 families at the five time points: one-month, six-months, 15-months, 24-months, and 36-months after childbirth. An Individual Growth Model, which incorporated fixed and random effects, was performed to investigate the trend of maternal depressive symptoms by taking into account variances of time, child general health, maternal social support, child sex, childcare, family income to needs ratio, mother’s age at child birth, and mother’s employment status.
Results: Findings from this study indicated that mothers had the highest level of depressive symptoms at one month after childbirth. The level of maternal depression decreased after one month, then remained at the same level until 24 months, and slightly increased at 36 months. Significant within-subject effects were indicated—this suggested that the trend and patterns of maternal depression varied over time by individual characteristics.
Conclusions: Individually specific intervention program and treatment plan may be more effective for maternal depressive symptoms than a universal program that intended to meet all women’s needs.

References:

NR306 Monday, May 3, 3:00 p.m.–5:00 p.m.
Neonatal Outcome Following Maternal Antenatal Depression and Anxiety
Supported by Pfizer Inc.
Liselott Anderson, M.D., Obstetrics and Gynecology Department, Sunderby Hospital S-971 80 Lulea, Sweden; Marie Bixo, Ph.D., Inger Sundstrom-Poroma, Ph.D., Monica Astrom, Ph.D., Marianne Wulff, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to treat maternal antenatal depression and consider the effect on neonatal outcome.

Summary:
The aim of this study was to determine the neonatal outcome in women with depressive and anxiety disorders during the second trimester of pregnancy in a population-based sample. Participants were 1,465 women and their neonates, born at two obstetric clinics in Sweden. The inclusion period for the women was from October 2, 2000, to October 1, 2001. The Primary Care Evaluation of Mental Disorders (PRIME-MD) was used to evaluate mental disorders in the second trimester of pregnancy. To assess demographic characteristics, birth statistics and birth-related complications, the medical records of the included women and their offspring were reviewed after delivery. The study results revealed no differences in neonatal outcome between women with antenatal depressive disorders and/or anxiety disorders and healthy subjects. In conclusion, neonatal outcome did not deteriorate despite the women’s mental health during pregnancy.

Funding Source(s): Ume University, Sweden; Swedish Society for Medical Research; Pfizer AB, Sweden.

References:

NR307 Monday, May 3, 3:00 p.m.–5:00 p.m.
Psychological Sequelae of the September 11th Terrorist Attacks: Preliminary Results From the World Trade Center Clean-Up and Recovery Health Assessment
Raz Gross, M.D., Department of Epidemiology, Columbia University, 600 West 168th Street, Room 518, New York, NY 10032; Alan Langlieb, M.D., Daniel Herman, Ph.D., Alison Geyh, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be familiar with the traumatic exposures and psychological outcomes of post-disaster clean up and recovery workers, and their relation with general health and impairment.

Summary:
Objective: To describe prevalence and correlates of PTSD, depression, and other mental disorders among clean-up and recovery workers at WTC site post 9/11.
Method: Mail survey sent between March and July of 2003 to 4,565 workers from three local unions and the New York City Department of Sanitation who were identified as having worked at the WTC site (exposed), and 2,103 workers from a subset of these organizations who did not work at the WTC site (“unexposed”).
Results: Response rate among exposed contact groups ranged from 22% to 34%. Response rate among unexposed ranged from 10% to 12%. Preliminary data indicate that approximately 75% of the respondents from the exposed group report symptoms consistent with psychological distress, probable anxiety disorders, depression, or PTSD. Prevalence of mental disorders and their correlation with exposure variables, general health measures, and sociodemographic characteristics will be presented.

Conclusions: According to our preliminary analysis, workers exposed to work on WTC site post 9/11 report symptoms consistent with high prevalence of psychological problems, approximately 22 months after the disaster. Such findings, though possibly inflated by selection bias, have important clinical and public health implications.

Funding Source(s): Supported by a grant from the National institutes of Environmental Health Sciences P30 ES0 3819-15S1

References:

NR309
May 3, 3:00 p.m.-5:00 p.m.
The Prevalence of Comorbid Depression and Anxiety Using the PHQ in Japan
Supported by Pfizer Inc.
Kumiko Muramatsu, M.D., Social Welfare Department, Niigata Seiryo University, Niishihata 589-32, Niigata City 9518104, Japan; Yoshiyuki Muramatsu, M.D., Fumitoshi Yoshimine, M.D., Hidehito Miyao, M.D., Elichi Suzuki, M.D., Kunitoshi Kamijima, M.D., Fumitoshi Yoshimine, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to define comorbid depression and anxiety, and comorbid subthreshold depression and subthreshold anxiety in primary care patients in Japan.

Summary:
Introduction: The purpose of this study was to detect the prevalence of mental disorders, especially concerning comorbid anxiety and depression in primary care settings in Japan.

Methods and Materials: A total of 800 adult patients were selected randomly and by convenience from seven primary care settings. The PHQ, a short, patient-completed version of the original PRIME-MD, was used to determine the presence of DSM-IV disorders.

Results: The prevalence of any mood disorders or any anxiety disorders was 11.38. 7.3% of the patients were diagnosed with mood disorders (major depression or other depressive disorders), which fully met the criteria. Subthreshold depression was diagnosed as minor depression by the PHQ. 4% of the patients were diagnosed with minor depression. 11.8% of the patients were diagnosed with anxiety disorders which fully met the criteria. 2.2% of the patients were diagnosed with anxiety disorder (NOS: Not Otherwise Specified). The Odds ratio for co-occurrence of any mood disorders with any anxiety disorders is 11.50 (95% CI: 6.12–21.6, 99% CI 5.09–26.36). The Odds ratio for co-occurrence of minor depression with anxiety disorders (NOS) is 8.00.

Funding Source(s): Educational grant from Pfizer US Pharmaceutical Inc.

References:

NR308
May 3, 3:00 p.m.-5:00 p.m.
Long-Term Mental Health Outcome of Breast Feeding
Joseph B.A. Meagher, M.D., Government and Politics, University of Manchester, Dover Street Building, Dover Street, Manchester M139PL, United Kingdom; Ircsima Leroi, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize breast feeding as a predictor of adult mental well-being.

Summary:

Objective: To examine the relationship between breast feeding in infancy and subsequent mental health outcomes in adulthood.

Methods: 17,196 births recorded in the UK over a period of one week in 1970 were the subjects of the 1970 British Cohort Study (BSC). The subjects’ mothers were interviewed about their breast feeding practices during the first three months of the subjects’ life. The last three follow-up waves of the study (1986, 1996, 2000) included administration of the Malaise Inventory (MI), a self-report scale of psychological well-being and stress, to the subjects during adolescence and early adulthood. The MI scores during these waves were examined in relation to breast feeding practices during infancy.

Results: Breast feeding for at least one month in infancy leads to significant decreases in levels of stress as measured by the MI longitudinally. Other variables associated with infancy, such as social class and pregnancy smoking status of the mother also predict levels of adult stress.

Conclusion: Breast feeding of at least one month’s duration during infancy predicts higher rates of psychological well being and reduced stress in adolescence and early adulthood.

References:

NR310
May 3, 3:00 p.m.-5:00 p.m.
Mixed Anxiety-Depressive Disorder in Primary Care: Incidence and Somatic Symptoms
Pedro Garcia-Parajua, M.D., Department of Psychiatry, Hospital Puerta De Hierro, San marín De Porres, 4, Madrid, Spain; Jorge Iglesias-Garcia, M.D., Lucía De Ugarte, M.D., Enrique Baca-Garcia, M.D., Luis Caballero, Ph.D., Enrique Baca, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should know data about incidence and clinical significance of a still not well-established syndrome that seems to be very common among primary care attendees.

Summary:

Introduction: To determine the incidence and somatic symptoms of the mixed anxiety-depressive disorder (MAD) in primary care.
Methods: 223 consecutive primary care patients aged 18–65 without known psychiatric illness were interviewed using the Prime-MD clinical evaluation guide and DSM-IV diagnostic criteria for MAD. Demographic data, somatic symptoms included in the patient Prime-MD questionnaire, medical diseases and treatments, and number of visits to the GP during the last year were also collected.

Results: 18 patients (7.8% [IC95%: 4.3-11.3%]) had a combination of subsyndromal anxiety and depressive features that fulfilled DSM-IV criteria for MAD: 20 (8.9% [IC95%: 5.4-12.5%]) patients had an anxiety disorder alone; 11 (4.9% [IC95%: 1.4-8.5%]) patients had a depressive disorder alone; and 30 patients (13.4% [IC95%: 9.9-16.9%]) had a comorbid anxiety and depressive disorder. Patients with MAD had less somatic symptoms than patients with a comorbid disorder (p=0.02), but more than patients with other psychiatric disorders (p=0.032) and patients without psychiatric morbidity (p<0.001).

Conclusions: The results show that there is a considerable subgroup of patients among primary care attendees suffering a subsyndromal anxiety and depressive disorder (MAD). Patients suffering a MAD have more clinical impairment, in terms of somatic symptoms, than patients without psychiatric morbidity or other psychiatric disorders.

References:

NR311 Monday, May 3, 3:00 p.m.-5:00 p.m.
Trauma Exposure and Psychopathology in African Americans
Tanya Alim, M.D., Howard University, 530 College Street, NW, Room 207, Washington, DC 20059; Dennis S. Charney, M.D., William B. Lawson, M.D., Barbara Williams, B.S., Ruth E. Graves, Ph.D., Bruce W. Smith, Kimberly Walton, Ph.D., Notaleomwan Agibogun, Elizabeth Brisbane, B.S.C., Jermaine Robertson, Ph.D., Billie Downing, B.S., Monique Golding, M.D., Jamie Hamilton, B.S.

Educational Objectives:
At the conclusion of this session, the participant should be able to identify risk and protective factors in African-American trauma survivors.

Summary:
Little data have been obtained on the effects of trauma and the development of psychopathology in the African-American population. It is largely unknown what the lifetime prevalence rates of trauma and disorders, such as PTSD, are in African-Americans.

Objectives and Aims: (1) to determine the prevalence of trauma and associated psychopathology in African-Americans attending primary care settings at Howard University (HU); (2) to assess patients for the prevalence of PTSD, depression, and other forms of psychopathology; (3) to identify risk and protective factors in trauma survivors with and without psychopathology.

Methods: Patients attending a primary care office were given a survey-assessing trauma, resilience and coping. Those experiencing significant lifetime trauma(s) were further evaluated using a comprehensive psychiatric assessment battery.

Findings: To date, 391 patients have been approached and 190 participants have agreed to participate. At least 67% report experiencing one significant psychological trauma according to DSM-IV criteria. Eighty-one percent have completed a comprehensive battery. Thirty-five percent met criteria for lifetime PTSD; 34% had a mood disorder and 54% met criteria for a substance use disorder. The risk and protective factors related to psychopathology will be presented at the meeting.

Funding Source(s): NIMH: HU MAP contract and Howard University FRSG grant

References:

NR312 Monday, May 3, 3:00 p.m.-5:00 p.m.
Relationship Between Anxious Depression and Treatment Outcome in Outpatients With Depression
Eliana Tossani, Ph.D., Psychiatry Department, Mass. General Hospital, 5 Long Fellow Place, 215 Room, Boston, MA 02114; Alessandra Mascarini, M.D., Jonathan E. Alpert, M.D., David Mischoulon, M.D., George I. Papakostas, M.D., Julie L. Ryan, B.A., Maurizio Fava, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the relationship between the presence of anxious depression and the outcome of antidepressant treatment in major depression.

Summary:
Objective: This study examines the relationship between anxious depression and treatment outcome among major depressive disorder (MDD) patients participating in a study comparing the antidepressant efficacy of a standardized extract of St. John’s wort with both placebo and fluoxetine.

Method: Following a one-week, single-blind, wash-out, patients with MDD diagnosed by SCID were randomized to 12 weeks of double-blind treatment with LI 160 St. John’s wort extract (900 mg/day), fluoxetine (20 mg/day), or placebo. The 17-item Hamilton Rating Scale for Depression (HAM-D-17) was the primary efficacy measure. While anxious depression was defined as having a baseline HAM-D anxiety/somatization factor score = or > 7, remission was defined as a HAM-D-17 score = or < 7 at endpoint. The ability of both anxious depression and the individual baseline HAM-D anxiety/somatization factor scores to predict treatment outcome were assessed separately for patients treated with active treatment (St. John’s Wort or fluoxetine) and placebo with a logistic regression method.

Results: 135 patients (57% women, mean age: 37.3 ± 11.0; mean HAM-D: 19.7 ± 3.2) were randomized to double-blind treatment and were included in the intent-to-treat analyses, and the remission rates were 38% in the St. John’s wort group, 30% in the fluoxetine group, and 21% in the placebo group. After adjusting for baseline HAM-D-17 scores (minus the anxiety/somatization items), anxious depression had significantly (p < .05) lower remission rates than nonanxious depression with active treatment, but not with placebo. When the six individual items of the HAM-D anxiety/somatization factor were assessed, only psychic and somatic anxiety significantly (p < .05) predicted poorer outcome with active treatment, again after adjusting for baseline HAM-D-17 scores (minus the anxiety/somatization items).

Conclusion: The presence of anxious depression and, in particular, of psychic and somatic anxiety, significantly predicted poorer outcome following antidepressant treatment, but such relationship was not present among the placebo-treated patients.

Funding Source: Lichtwer
NR313  Monday, May 3, 3:00 p.m.-5:00 p.m.
Methodological Considerations in a GAD Treatment Trial
Supported by Pfizer Inc.
Rebecca G. Knapp, Ph.D., Biometry and Epidemiology Department, Medical University of South Carolina, 171 Ashley Avenue PO Box 250835 Charleston, SC 29425; Olga Brawman-Mintzer, M.D., Elizabeth Slate, Ph.D., Hai Lin, B.S.

Educational Objectives:
At the conclusion of this session, the participant should be able to describe the approximate impact of a placebo run-in design element on effect size and potential effects on generalizability of study results in a GAD treatment study.

Summary:
Objective: Traditional registration clinical trials frequently incorporate approaches, such as a placebo run-in period, designed to boost the effect size. We investigated the potential effect of a placebo run-in design element on clinical trial results in subjects with DSM-IV generalized anxiety disorder (GAD).

Methods: Data from a multicenter, 10-week, placebo-controlled, flexible dosing trial of sertraline (50–200mg/d) in GAD subjects that did not utilize placebo run-in period, were used. To approximate a placebo run-in, a data subset comprising subjects who experienced < 20% decline in HAM-A total scores during study week 1 (at half minimal dose) was created. Results for full ITT data set (n=326) were compared with the subset to evaluate the impact of elimination of hypothesized placebo responders on treatment effect sizes and statistical significance.

Results: The placebo run-in approximation demonstrated a larger effect size and smaller p-values on all main outcome variables and lower placebo response rate compared with the full sample despite a 42% reduction in sample size (n=190).

Conclusion: Results indicate a potential for an artificially enhanced treatment effect with a placebo-run in period. These results have implications for generalizability to a general clinical population from standard, placebo run-in design utilized in corporate-sponsored, registration trials.

Funding Source(s): Investigator Initiated Grant to Dr. Brawman-Mintzer from Pfizer Pharmaceutical Co.

References:

NR314  Monday, May 3, 3:00 p.m.-5:00 p.m.
Prevalence and Impact of Anxiety Disorder Comorbidity in Schizophrenia
Raphael J. Braga, M.D., Research Department, Hillside Hospital, 75-59 263 Street, Glen Oaks, NY 11004; Mauro V. Mendelowicz, M.D., Rogerio Marrocos, M.D., Ivan L.V. Figueira, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize the possibility of co-occurrence of anxiety disorders in patients with schizophrenia and its possible implications.

Summary:
Only two clinical studies described the presence of all anxiety disorders in patients with schizophrenia, and the impact of this co-occurrence remains unclear. In the present study, 53 patients from a Brazilian sample with a diagnosis of schizophrenia were interviewed: (1) to determine the prevalence of comorbid anxiety disorders; and (2) to compare the group of patients with comorbid anxiety to those without comorbidity regarding psychopathology, disability, and quality of life. Anxiety diagnoses were made with the SCID-DSM-IV. The patients were also assessed with the BPRS, SCL-90, SF-36, and the Sheehan Disability Scale (SDS). Anxiety comorbidity was present in 41.5% of the patients, and the most common diagnoses were social phobia (17%), obsessive-compulsive disorder (15.1%), and generalized anxiety disorder (9.4%). Disability, as measured by the SDS, was significantly higher among patients with anxiety comorbidities. No other measures were found to be different. Hence, anxiety disorder comorbidity was a prevalent phenomenon in the sample studied, and appears to worsen the level of disability in schizophrenia.

References:

NR315  Tuesday, May 4, 12:00 p.m.-2:00 p.m.
Open-Label Add-On Quetiapine for Bipolar Depression: An Eight-Week Trial
Roumen V. Milev, M.D., Department of Psychiatry, PCC, Mental Health Services, 752 King Street West, PO Box 603, Kingston, ON K7L 4X3, Canada; Gaby Abraham, M.D., Fia Voutsilakos, M.D., Paul Hoaken, M.D.

Educational Objectives:
At the conclusion of this session, the participant should: (1) be aware of the use of add-on quetiapine for patients with bipolar depression; and (2) be able to improve the outcome of treatment.

Summary:
Objective: Bipolar disorder is a common, chronic and disabling condition. While at least one third of the time patients are depressed, they do not always respond to mood stabilizers. Attempts to treat them with antidepressants can provoke a switch to mania or increase the cycling pattern. With increasing number of reports suggesting that atypical antipsychotics are helpful, this study tests the role of quetiapine in achieving response.

Method: An open-label trial to assess the response of patients with bipolar depression to add-on quetiapine to their usual treatment. Currently depressed (HAM-D > 18), bipolar I or II patients, who were 18 years or older, and no change of antidepressants > 3 weeks were enrolled. Quetiapine was added openly and the dose increased as tolerated, mean daily dose at eight weeks 250 mg, range 50–400 mg. Outcome measures were HAM-D, YMRS, CGI-Severity and AIMS at entry, four and eight weeks.

Results: Eight patients are enrolled so far in this ongoing study, 3 males and 5 females. Five patients completed week 8. HAM-D21 fell by 17.8 points at week 4 and by 22.6 at week 8 and CGI-Severity by 1.8 and 2.6 respectively. There were no major side effects.
Conclusions: Add-on quetiapine is effective and well tolerated in patients with bipolar depression.

References:

NR316 Tuesday, May 4, 12:00 p.m.–2:00 p.m.
Exposure to Lithium Enhances Synaptic Plasticity in the Hippocampus
Seong-Sool Shim, M.D., Psychiatry Department, Case Western Reserve University, Hanna Pavilion, 1100 Euclid Avenue, Cleveland, OH 44106; Rebecca Russell, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should: (1) recognize lithium enhances synaptic communication leading to restore impaired neuronal circuits involved in the pathophysiology of bipolar disorder; and (2) understand that this cellular mechanism is associated with the therapeutic efficacy of lithium.

Summary:
Recently, lithium has been found to exhibit neuroprotective and neurotrophic actions by influencing gene expression of cyclic adenosine monophosphate response element-binding protein (CREB), Bcl-2, and brain-derived neurotrophic factor (BDNF). These factors have shown to increase dendritic proliferation, prohibit apoptosis and enhance synaptic efficacy. In this way lithium might affect synaptic plasticity. This was investigated in the hippocampus of rats that received either lithium chloride (1 mEq) or vehicle (PBS) injections (IP) for two weeks. At the endpoint, the hippocampus was stained with Golgi Staining method to examine the effects of lithium on proliferation of dendrites and dendritic spines in the dentate gyrus (DG) and area CA1. Field excitory post-synaptic potential (fEPSP) and population spike (PS) were measured in DG in hippocampal slices to examine the effects of lithium on synaptic plasticity as determined an input/output (I/O) curve, a paired-pulse (PP) paradigm and long-term potentiation (LTP). Two weeks of 1mEq, lithium IP increased the dendritic proliferation and the density of dendritic spines, and produced a significantly steeper I/O curve, increased LTP and decreased PP inhibition in DG. This study provides morphological and electrophysiological evidence that exposure to lithium increases synaptic efficiency and synaptic plasticity in the hippocampus.

References:

NR317 Tuesday, May 4, 12:00 p.m.–2:00 p.m.
Effects of Psychotropics on HbA1c in a Cohort of Bipolar Patients
Supported by GlaxoSmithKline
Ruby C. Castilla-Puentes, M.D., Epidemiology Research and Development, GlaxoSmithKline, 5 Moore Drive, Triangle Park, NC 27709; Bobbie Coleman, M.S., Leo Russo, Ph.D., Thomas R. Thompson, M.D., Robert A. Leadbetter, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to identify the effect of psychotropics on HbA1c concentrations in bipolar patients.

Summary:
Objective: Research suggests that certain psychotropics may induce glucoregulatory dysfunction. Hyperglycemia increases levels of HbA1c. This study investigated the relationship between psychotropic use and concentration of HbA1c in bipolar patients.
Method: Analysis was conducted of 76,671 bipolar patients from Integrated Healthcare Information Services. A total of 381 patients with at least two measures of HbA1c from January 1997-June 2002 were included. We compared HbA1c levels from first to last HbA1c measurement. Patient characteristics and type of psychotropic medication were examined.
Results: 30 used antipsychotics, 24 mood stabilizers (anticonvulsant), 10 lithium, 51 antidepressants, 116 combinations, and 150 patients used no psychotropics. HbA1c levels declined significantly in both patients taking (mean, SD 7.4 ± 2.0% vs. 6.9 ± 1.8%, p=0.001) or not taking psychotropics (7.5 ± 2.1% vs. 6.9 ± 1.8%, p=0.001). The only exception to this trend was among patients taking antipsychotics where there was a slight increase during this period (7.0 ± 1.8% vs. 7.2 ± 3.7%, p=NS).
Conclusions: Mood stabilizers (anticonvulsants) antidepressants and lithium in monotherapy and combination were associated with a decrease in HbA1c levels. Although not statistically significant, antipsychotics were associated with an increase in HbA1c in this population. Further studies are needed to examine the effects of psychotropics on glucose regulation in bipolar patients.

Funding Source(s): GlaxoSmithKline

References:

NR318 Tuesday, May 4, 12:00 p.m.–2:00 p.m.
Serotonin Transporter mRNA Is Reduced in Lymphocytes of Major Depression Patients
Lucimey Lima, Neuroquimica, IVIC, Altos de Pie APDO 21827, Caracas 1020A, Venezuela; Salvador Mata, M.D., Mary Urbina, MSC, Alfonso Gonzalez, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to comprehend nervous-immune interactions.

Summary:
Serotonin transporter (5-HTT), by the binding of [3H]paroxetine, is reduced in lymphocytes of depressed patients. The aim of this research was to evaluate the levels of 5-HTT mRNA by RT-PCR using the primer of human 5-HTT -1416 to -1397 and -910 to -889, and to localized 5-HTT using a specific antibody with a second anti-lgG-FITC, Blood was obtained and lymphocytes isolated by Ficoll/Hypaque gradients. Twenty-nine patients (33 years, 4 men) with a major depression episode, free of medication, without other disorder of Axis I or II, were selected by DSM-IV criteria. The score for the severity, by Hamilton Scale, was 33. Thirty controls (37 years, 4 men) also participated. The gene regulatory region polymorphism 5-HTTLPR was detected in patients and controls (9%), others presented only L-allele (60 and 73% in pa-
tients and controls) or S-allele. There was a significant reduction in L form of depressed respecting controls (1.70 vs. 3.14 equivalents/μg of RNA). A significant and negative correlation was observed between the levels of S form and the severity. The percentage of lymphocytes with intense fluorescence was 8% and 20% for patients and controls. The reduction in the number of 5-HTT reported in lymphocytes of major depression patients could be due to decreased mRNA and reduced number of cells expressing the transporter.

Funding Source(s): FONACIT G-1387, Venezuela

References:

NR319  Tuesday, May 4, 12:00 p.m.–2:00 p.m.
NMS, Serotonin Syndrome, and Lethal Catatonia: Frequency and Detection
Brendan T. Carroll, M.D., Neuroscience Alliance, 330 Taylor Blair Road, West Jefferson, OH 43162

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the major motor signs that comprise the lethal catatonic syndrome, serotonin syndrome (SS), and neuroleptic malignant syndrome (NMS) and their uncommon occurrence.

Summary:
The frequency and nosology of lethal catatonia has been elaborated in the last century. The psychopathological and methodological issues pertaining to lethal catatonic syndrome (LC), neuroleptic malignant syndrome (NMS), and serotonin syndrome (SS) and have been raised in the 1980s and 1990s, respectively. Yet, these disorders are relatively rare. In an effort to address the frequency of these syndromes, a retrospective review of one neuropsychiatric institution was undertaken. This also included the reporting of these cases to outside clinical entities. A survey of the members of The Neuroscience Alliance was conducted to determine how frequently these entities were encountered by neuropsychiatry practitioners. In one institution over eight years there were as follows: LC-2, NMS-2, SS-2 and other hyperthermic syndrome-2. One case of LC was called into NMSIS (an NMS Information Service) and one case of SS was reported to the FDA. The Neuroscience Alliance Survey revealed a frequency of less than one case per five years of clinical practice of either LC, NMS, SS, or related syndromes. Thus, the idea of distinguishing between these syndromes becomes a challenge given their low frequency of occurrence.

NR320  Tuesday, May 4, 12:00 p.m.–2:00 p.m.
Obsessive-Compulsive Symptoms Among Patients With Sydenham Chorea
Fernando R. Asbahr, M.D., Psychiatry Department, University of Sao Paulo, Rua Ovidio Pires de Campos S/N, Sao Paulo, SP 05403-010, Brazil; Lisa A. Snider, M.D., Marjorie Garvey, M.D., Dirce M.T. Zanetta, M.D., Helio Elkis, M.D., Susan Swedo, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize distinct clinical profiles of obsessive-compulsive symptoms in patients with Sydenham chorea and tic disorders, both conditions associated with dysfunction in the basal ganglia.

Summary:
Objective: This investigation documents the phenomenology of the obsessive-compulsive symptoms (OCS) among patients with Sydenham chorea (SC), a movement disorder associated with the onset of OCS. Among patients with tic disorders, a distinctive clinical profile of OCS has been described. We hypothesized that the OCS associated with SC would have a profile similar to the one reported in patients with tics.

Method: Seventy-three patients with SC who had OCS were assessed with the Yale-Brown Obsessive-Compulsive Scale Checklist at the University of Sao Paulo Medical Center in Sao Paulo, Brazil (N=45) and at the National Institute of Mental Health in Bethesda, Maryland (N=28), and its 12 main symptom categories were factor analyzed by using principal-components analysis.

Results: The analysis yielded a five-factor solution, which accounted for 64.46% of the total variance: contamination/cleaning/symmetry, hoarding/ordering, checking/repeating compulsions, counting and religious obsessions, and aggressive/somatic obsessions.

Conclusions: The clinical profile of OCS in our sample was not the same as the one that have been reported in patients with tic disorders. However, our sample consisted of children aged 7–12 years and previous reports are from adults with tics. The symptomatology observed in our sample was similar to the one reported in youngsters with obsessive-compulsive disorder.

Funding source(s): Partially supported by FAPESP (Fundação de Amparo à Pesquisa de Estado de São Paulo, Brazil) grant 01/07985-5 to Dr. Asbahr

References:
Educational Objectives:

At the conclusion of this session, the participant should be able to evaluate the effect of escitalopram and citalopram in the speed of recovery of rat dorsal raphe neurons.

Summary:

Introduction: Of the selective serotonin (5-HT) reuptake inhibitors available, escitalopram presents the highest selectivity in inhibiting 5-HT reuptake. We investigated if the higher selectivity of escitalopram versus citalopram affected its electrophysiological properties in rats.

Results: At the presynaptic level, escitalopram was four times as potent as citalopram (single dose, i.v.), in suppressing the firing activity of dorsal raphe neurons (DRNs). A seven-day treatment with escitalopram (10mg/kg/day, s.c.) or citalopram (20mg/kg/day, s.c.) significantly decreased the spontaneous firing activity of DRNs (by 61 and 70%, respectively). This firing activity returned to normal after two weeks treatment with escitalopram versus three weeks for citalopram. This recovery of DRN firing was associated with a desensitization of somatodendritic 5-HT receptors. After two days of treatment with escitalopram and two weeks with citalopram, the administration of the selective 5-HT1A receptor antagonist WAY-100,635 dose-dependently increased the firing activity of dorsal hippocampus CA1 pyramidal neurons, revealing an enhanced tonic activation of postsynaptic 5-HT1A receptors.

Conclusions: Although both escitalopram and citalopram disassociate CA1 pyramidal neurons, the present study shows that escitalopram produces a faster recovery of 5-HT neuronal firing activity than an equivalent dose of citalopram. These results may explain the faster onset of efficacy of escitalopram versus citalopram.

This research was funded by a grant from H. Lundbeck A/S.

References:


NR322 Tuesday, May 4, 12:00 p.m.–2:00 p.m.

Tolerance to Somnolence With Quetiapine: Preclinical Mechanisms and Clinical Evidence Supported by AstraZeneca Pharmaceuticals

Jeffrey M. Goldstein, Ph.D., AstraZeneca, 1800 Concord Pike, PO Box 15437, Wilmington, DE 19850-5437; Kate Zhong, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to: (1) characterize the incidence and severity of somnolence in patients treated with quetiapine; and (2) to explain why somnolence is generally a transient effect in terms of this agent's binding characteristics at H1 receptors.

Summary:

Objective: Somnolence is common in patients taking antipsychotics, but may be transient in patients taking quetiapine because of its receptor binding properties. Quetiapine blocks H1 receptors (responsible for somnolence) at lower doses than D2 receptors (responsible for antipsychotic effects). At doses up to 800 mg/d, the blockade of H1 receptors may contribute in the rapid development of tolerance. The objective was to determine the incidence, severity, and dose-relatedness of somnolence in patients treated with quetiapine.

Methods: Data from 76 trials (12 placebo-controlled) were analyzed retrospectively for reports of somnolence as adverse event, including first onset, severity, and resultant withdrawals.

Results: Among 7894 patients with varying diagnoses treated with quetiapine, 25.5% reported somnolence; 62% resolved by treatment and. Somnolence was mild or moderate in 94.9% of cases: incidence decreased from 15.5% in week 1 to 8.6% in week 6. Only 1.3% of patients withdrew because of somnolence. Somnolence was not dose related.

Conclusions: Results suggest that when daytime somnolence occurs in patients taking quetiapine, rapid tolerance developed by the drug at the H1 receptor produces transient, mild to moderate somnolence that is not dose-related and rarely results in treatment discontinuation.

Funding Source(s): The research reported here was supported by AstraZeneca Pharmaceutical LP.

References:


NR323 Tuesday, May 4, 12:00 p.m.–2:00 p.m.

A Major SNP Haplotype of the Arginine Vasopressin 1B Receptor Protects Against Recurrent Major Depression

Stephan Claes, M.D., Molecular Genetics, University of Antwerp, Universiteitsplein 1, Wilrijk 2610, Belgium; Dirk Van West, M.D., Jurgen Del-Favero, Ph.D., Julian Mendlewicz, M.D., Rolf Adolfsson, Christine Van Broeckhoven

Educational Objectives:

At the conclusion of this session, the participant should be able to evaluate the evidence implicating the AVP receptor 1B gene in the genetic vulnerability for major depressive disorder.

Summary:

An increasing amount of evidence suggests that affective disorders might be related to dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis, one of the stress-response systems. Arginine vasopressin (AVP) influences several symptoms, relevant to affective disorders, notable memory processes, pain sensitivity, synchronization of biological rhythms, and timing and quality of REM sleep. We examined whether genetic variations in the arginine vasopressin receptor 1b gene (AVPR1b) could be associated with increased susceptibility to affective disorders using a gene-based association analysis of single nucleotide polymorphisms (SNPs). Five SNPs were identified in AVPR1b and genotyped in two well-diagnosed samples of 92 patients with recurrent major depressions and matched controls. In the Swedish sample, we observed significant allele (p = 0.02) and genotype (p = 0.01) association with SNP AVPR1bs5; in the Belgian sample a borderline significant association with SNP AVPR1bs5 (p = 0.04). In both patient-control samples the haplotype defined by alleles A T C A G for the AVPR1b SNPs s1 s2 s3 s4 s5 was significantly (p < 0.001) overrepresented in controls compared to patients. Our data support a protective effect of this major haplotype to develop recurrent major depression.

References:


NR324 Tuesday, May 4, 12:00 p.m.–2:00 p.m.
Pharmacogenetic Predictors of Lithium Response in Bipolar Disorder
Rebecca A. McKinney, B.A., Psychiatry Department, University of California, San Diego, 8950 Villa La Jolla Drive, Suite A203, La Jolla, CA 92037; Janet Abou, B.S.; Tatiana Shekhman, B.S.; Meghan Alexander, B.S., Geraldine Smith, John R. Kelsoe, Jr., M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to demonstrate a working knowledge of certain genetic predictors of lithium response. It should also be clear that pharmacogenetics research is integral to the development of useful screening tests for medication treatment of mood disorders.

Summary:
Objective: Pharmacotherapy in bipolar disorder has greatly improved, but the high level of variability in individual drug response still leaves some guesswork. As a result, a wide variety of studies have been conducted to explore potential clinical and biological predictors of drug response, particularly in lithium. Genetic factors likely play an important role in determining therapeutic lithium response and are the primary focus of this study. Two genes in particular, the serotonin transporter (HTT) and inositol polyphosphate 1-phosphotase 1-phosphotase (INPP1), have been previously reported to predict lithium response.

Methods: 92 lithium responders and 92 non-responders were identified from a large sample of subjects collected for genetic linkage studies of bipolar disorder. Each subject was assessed for lifetime lithium response using the lifechart method, patient subjective ratings, and medical records. Over 70 SNP markers were genotyped using a 5′ exonuclease assay. Two repeat markers in the HTT gene, a promoter repeat (HTTLPR) and an intron 2 repeat, were also genotyped using fluorescent detection.

Results: These data are being analyzed for their ability, individually and in combination, to predict lithium response. These will be presented.

Conclusions: A panel of genetic variants capable of predicting lithium response would be of immense clinical value in facilitating the treatment of bipolar disorder.

References:

NR325 Tuesday, May 4, 12:00 p.m.–2:00 p.m.
The Relations Between Clozapine Response and CYP1A2 Gene Polymorphism
Cengiz Basoglu, M.D., Psychiatry Department, Gata Hbasa Hospital, Kadikoy, Istanbul 81327, Turkey; Hakan Balibey, M.D., Mesut Cetin, M.D., Umit Basar Seniz, M.D., Servet Ebrinc, M.D., Unit Yasar

Educational Objectives:
The aim of this study was to investigate the CYP1A2*1F mutated allele and its response to clozapine treatment in the patients with schizophrenia.

Summary:
Objective: The relation between response to clozapine treatment and CYP1A2 genetic polymorphism (CYP1A2*1F C→A mutation), in the patients with schizophrenia was investigated.

Methods: Patients were assessed with BPRS, SAPS, SANS and routine biochemical assessment. Subjects were followed for 18 weeks. Measurements were before and after the treatment, respectively, on the first and 18th weeks. Clozapine was given in the range 200 to 600 mg/day. Patients with a prior clozapine usage were assessed as a retrospectively. Ninety seven of 100 patients completed the study. Two patients had a heavy sedation and one patient refused to give blood for the following treatment and thus these three patients were dropped from the study.

Results: After the completion of the 18th week, a positive response defined as a 20% increase in the BPRS, SANS, SAPS scores compared to the values before the treatment.

Conclusions: In the patients who had taken to the clozapine treatment before with CYP1A2*1F (C→A mutation) polymorphism, the response to clozapine treatment was less than the expected result. This difference was found to be statistically significant (p<0.05).

References:

NR326 Tuesday, May 4, 12:00 p.m.–2:00 p.m.
Association of DBH Gene and Phenotypic Variation in Korean Patients With Schizophrenia
Jinkyung Park, M.D., Psychiatry Department, Armed Forces Hospital, Chungpyeong-ri, Gyeonggi-do, Seoul 477-815, South Korea; Yongseon Shin, M.D., Jiyoung Song, M.D., Jongwoo Kim, M.D., Heejae Lee, M.S., Ahrang Cho, M.D., Mikyung Kim, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize that the DBH gene may be involved in modifying the psychiatric symptoms of schizophrenia and the time of developing schizophrenia.

Summary:
Objective: The structural gene encoding the enzyme dopamine beta-hydroxylase (DBH) is closely related to the DBH activity and to psychotic symptoms in several psychiatric disorders. This study examined association between three polymorphisms (DBH5'-ins/del, DBH-1021c/t, and DBH 444g/a) of the DBH gene and phenotypic variation in Korean schizophrenics.

Method: Allelic and haplotype distributions of these three polymorphisms using restriction fragment length polymorphism were compared between 161 Korean controls and phenotypic groups of 140 Korean schizophrenics stratified according to gender, subtype, and onset age.

Results: The genotype and allele frequencies of DBH 444g/a polymorphism showed significant differences between the group of disorganized type schizophrenics and the controls (X²=24.977, df=2, p=0.002; X²=5.613, df=1, p=0.029). Significant differences were found between the group of schizophrenics whose onset age is under 20 and the controls in the genotype distribution of DBH 444g/a polymorphism (X²=7.402, df=2, p=0.03). The Ins-g haplotype was significantly more common in the group of disorganized type schizophrenics than in the controls (X²=11.42, df=3, p=0.01).
Conclusions: These results suggest that the DBH gene may be involved in modifying the psychiatric symptoms of schizophrenia and the time of developing schizophrenia.

References:

NR327 Tuesday, May 4, 12:00 p.m.–2:00 p.m.
Genetic Markers for Social Phobia in Patients Treated With SertralineSupported by Pfizer Inc.
Michael Liebowitz, M.D., Anxiety Disorders Department, New York State Psychiatric, 1051 Riverside Drive, New York, NY 10032; Hakan Sakul, M.D., Kathryn Durham, Ph.D., Cathryn M. Clary, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to understand the genetic variants in patients with generalized social phobia and recognize how response to sertraline is affected by genotype.

Summary:
Background: Social phobia (SP) is a chronic anxiety disorder with prevalence rates of 8% to 13%. Family and twin studies provide evidence that SP is a heritable trait with significant genetic influence.

Methods: This study is the pharmacogenomics sub-study of a multi-center, double-blind, placebo-controlled trial of sertraline for acute treatment of DSM-IV Generalized SP (Liebowitz et al., 2003). The primary objective was to explore correlations between efficacy endpoints and genetic markers located in the autosomal genome and the X-chromosome. Two hypotheses were tested: (1) sertraline vs. placebo treatment effect differs by genotype, and (2) within-treatment groups genotype is associated with differential response.

Results: Among the autosomal loci investigated, the GABRA2/G-142 polymorphism appears to have an effect on Sertraline vs. Placebo treatment (p=0.03, using LSAS). This may be due to an effect on Sertraline response (p=0.03, LOCF, using LSAS; p=0.01, LOCF, using CGI). Among the X-chromosome loci investigated, markers in the HTR2C gene may influence treatment effect size for women, possibly due to an effect on placebo response. Male subjects’ X-chromosome results may indicate an effect of GABRA3 markers on response.

Conclusion: Further analyses are in progress to fully evaluate these results. Findings from this study will contribute to our understanding of genetic mechanisms underlying social phobia.

References:

NR328 Tuesday, May 4, 12:00 p.m.–2:00 p.m.
5-HT6 and Response to Antidepressant Treatment in Major Depression
Seung-Hwan Lee, M.D., Department of Psychiatry, Inje University Paik Hospital, 2240 Daehwa-Dong Iisan-gu, Goyang 411-706, South Korea; Kang-Joon Lee, M.D., Young-Jo Chung, M.D., Heon-Jeong Lee, M.D., Byung-Joo Ham, M.D., Seung-Ho Ryu, M.D., Min-Soo Lee, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to determine if a 5-HT6 receptor polymorphism is associated with antidepressant treatment response in major depressive disorder.

Summary:
Introduction: The serotonin 6 (5-HT6) receptor is one of the newest candidate genes for the study of major depressive disorder (MDD) because it is abundant in the limbic system and some antidepressants have high affinity for it. But only a few association studies of 5-HT6 polymorphism and MDD have been published, and there were no positive results from MDD without comorbid disorder. The purpose of this study was to determine if a 5-HT6 receptor polymorphism is associated with antidepressant treatment response in MDD.

Methods: Ninety-one patients with MDD were evaluated after an eight-week treatment period and compared with 127 normal control subjects. The severity of depression was assessed using the 21-item HAM-D. Patients with other medical and psychiatric disorders were excluded. A polymerase-chain-reaction-based method was used for genotyping.

Results: An association analysis revealed no differences in genotype and allele distribution between patients with MDD and normal control subjects. However, there were significant differences in the treatment response in some HAM-D scores (sleep, activity, somatic anxiety, and total) between genotypes. Moreover, heterozygotes (CT genotype) showed significantly better treatment response than homozygotes (CC + TT genotypes), especially in the somatic-anxiety subcategory and the total score of HAM-D.

Conclusions: These findings imply that a 5-HT6 receptor polymorphism (C267T) is associated with treatment response in MDD.

References:

NR329 May 4, 12:00 p.m.–2:00 p.m.
Antipsychotic-Induced Weight Gain: Pharmacogenetics and Leptin Dysfunction
Gavin P. Reynolds, Ph.D., Biomedical Science Department, University of Sheffield, Western Bank, Sheffield, UK S10 2TN, United Kingdom; Lucy A. Templeman, Ph.D., Belen Arranz, M.D., Luis San, M.D.

Educational Objectives:
At the conclusion of this session, the participant should understand that genetic factors via their influence on leptin, a hormone controlling food intake, play a key role in determining weight gain, a major side effect of antipsychotic drug treatment.

Summary:
Objective: Increased body fat, leading to further morbidity and poor treatment adherence, is a common consequence of treat-
ment with antipsychotic drugs. We have found that a common genetic polymorphism of the 5-HT2C receptor promoter region has a strong influence on antipsychotic-induced weight gain in first-episode Chinese Han subjects. We hypothesised that this association is also true in first-episode Caucasian subjects with schizophrenia, and investigated the relationship with blood levels of the anorexigenic hormone leptin.

**Method:** We determined the association of the -759C/T 5-HT2C receptor gene polymorphism with antipsychotic-induced weight gain in a Spanish population with schizophrenia. Patients were monitored for weight, from which was calculated body-mass index (BMI), and blood leptin concentrations at six weeks and three months following treatment for a first psychotic episode and genotyped for the polymorphism.

**Results:** Patients carrying the T allele (n=11/12) showed less weight gain than those without (n=39) at 6 weeks (mean BMI change 1.00 vs 1.88 kg/m², p=0.02) and at three months (1.24 vs 2.68 kg/m², p=0.01). In a subgroup of 19 patients receiving olanzapine treatment, the effect remained significant at both time-points. Following antipsychotic treatment, patients exhibited a sustained increase in leptin concentrations, which was apparent in both genotype groups. Those with the T allele showed significantly higher leptin concentrations prior to treatment (7.5 vs 3.6 ng/ml, p=0.01), an effect that was independent of sex and initial BMI.

**Conclusion:** These findings demonstrate that the value of the 5-HT2C genotype in predicting antipsychotic drug-induced weight gain extends to a European population, and that the mechanism may involve effects on the function of the food intake regulating hormone leptin.

**References:**

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**NR330 Tuesday, May 4, 12:00 p.m.–2:00 p.m.**

**5HT2A Gene Polymorphisms in Different Psychiatric Disorders**

Sara Martinez, Ph.D., Psychiatry Department, Oviedo University, Julian Claveria 6-3, Oviedo 33006, Spain; Teresa Bascaran, M.D., Begona Paredes, M.D., Pilar A. Saiz, Ph.D., Blanca Morales, M.D., Maria P. G-Portilla, Ph.D., Julio B. Bobes, M.D.

**Educational Objectives:**
At the conclusion of this session, the participant should be able to recognize and discuss the role of two serotonin gene polymorphisms in the genesis of DSM-IV psychiatric disorders schizophrenia, OCD, suicidal behavior, and panic disorder.

**Summary:**
**Objective:** To investigate the role of two 5HT2A gene polymorphisms (T102C and A-1438G) in different psychiatric disorders, using DSM-IV criteria (schizophrenia, OCD, suicidal behaviour, and panic disorder).

**Patients and Method:** We genotyped 181 schizophrenic outpatients [mean age (SD)= 35.41 (11.31); males=58.6%], 74 OCD patients [mean age (SD)= 34.74 (10.43); males= 39.2%], 90 parasuicidal patients [mean age (SD)= 35.06 (11.79); males= 37.8%], 89 with panic disorder [mean age (SD)= 32.41 (8.22); males= 31.5%], and 144 healthy controls [mean age (SD)= 43.06 (11.21); males= 66.0%] from Asturias (Northern Spain) (same ethnic background).

Polymorphisms were determined after PCR amplification followed by digestion with the restriction enzyme Mspl and electrophoresis on an agarose gel.

**Results:** Both 5HT2A polymorphisms are in complete linkage disequilibrium in our population. The 5HT2A genotypes were in the Hardy-Weimberg equilibrium in patients and healthy controls. Genotype frequencies did not differ between patients and controls (p=0.348). However, an increased frequency of T102 (and, A-1438) carriers was found in schizophrenic outpatients compared with controls (p= 0.027; OR = 1.44; 95% CI= 1.05 1.96).

**Conclusions:** Polymorphic variations at 5HT2A gene could be associated with an increased risk of schizophrenia in our population.

**References:**

**NR331 Tuesday, May 4, 12:00 p.m.–2:00 p.m.**

**TNF-β Gene Polymorphism May Not Be Associated With Bipolar Disorder**

Tae-Youn Jun, M.D., Department of Psychiatry, St. Mary’s Hospital, 62 Yoido-dong, Youngdeungpo-gu, Seoul 150-713, South Korea; Kyong-Uk Lee, M.D., Won-Hee Lee, M.D., Jeong-Ho Chae, M.D., Won-Myong Bahk, M.D., Kwang-Soo Kim, M.D.

**Educational Objectives:**
At the conclusion of this session, the participant should recognize tumor necrosis factor-β gene polymorphism may not be associated with bipolar disorder in the Korean population.

**Summary:**
**Objectives:** Alterations of the immune system in patients with bipolar I disorder have been also proposed to date. And tumor necrosis factor (TNF)-β has been implicated in the regulation of immune system. The TNF-β gene is located within the class III region of the major histocompatibility complex on the short arm of chromosome 6. And it is known to show biallelic polymorphism (G to A transition), at position +252 in the first intron of TNF-β gene, and which is recognized by Nco I restriction enzyme. We investigated the association of TNF-β gene polymorphism in the Korean patients with bipolar I disorder.

**Methods:** 89 Korean patients diagnosed with bipolar I disorder according to DSM-IV and 202 normal healthy controls participated in this study. DNA was extracted from whole blood using proteinase K. Genotyping for TNF-β polymorphism was performed by PCR-RFLP method.

**Results:** Distribution of the alleles and genotypes in patients with bipolar I disorder was not significantly different from those of controls.

**Conclusions:** In conclusion, these results suggest that the polymorphisms of TNF-β gene are not involved in the pathophysiology of bipolar disorder in the Korean population.

**References:**
NR332  Tuesday, May 4, 12:00 p.m.-2:00 p.m.
Polymorphisms of IL-4 and IL-4-RX Gene for Affective Disorder in Koreans

Tae-Youn Jun, M.D., Department of Psychiatry, St. Mary's Hospital, 62 Yoido-dong, Youndeungpo-gu, Seoul 150-713, South Korea; Kyoung-Uk Lee, M.D., Jeong-Ho Chae, M.D., Won-Myong Bahk, M.D., Kwang-Soo Kim, M.D.

Educational Objectives:
At the conclusion of this session, the participant should understand polymorphisms of interleukin-4 promoter and receptor gene for affective disorder in the Korean Population.

Summary:
Objectives: We investigated the interleukin (IL)-4 promoter gene -590 and receptor alpha (Ra) gene 1902 polymorphism in the Korean patients with major depressive disorder and bipolar I disorder.

Methods: 110 patients diagnosed with major depressive disorder and 90 patients diagnosed with bipolar disorder according to DSM-IV and 185 normal healthy controls participated in this study. DNA was extracted from whole blood using proteinase K and the IL-4 promoter and receptor gene was amplified by polymerase chain reaction. The genotype was determined using single strand conformation polymorphism (SSCP) analysis.

Results: Distribution of the alleles and genotypes in patients with major depressive disorder and bipolar I disorder was not significantly different from those of controls.

Conclusions: In conclusion, these results suggest that the polymorphisms in IL-4 and IL-4-RX gene are not involved in the pathophysiology of major depressive disorder in the Korean population.

References:

NR333  Tuesday, May 4, 12:00 p.m.-2:00 p.m.
No Association of TAP2 Gene Polymorphism With MDD

Tae-Youn Jun, M.D., Department of Psychiatry, St. Mary's Hospital, 62 Yoido-dong, Youndeungpo-gu, Seoul 150-713, South Korea; Kyoung-Uk Lee, M.D., Song Jung-Min, M.D., Jeong-Ho Chae, M.D., Won-Myong Bahk, M.D., Kwang-Soo Kim, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to understand that there is no association of TAP2 gene polymorphism with major depressive disorder

Summary:
Objectives: The genes for transporters associated with antigen processing (TAP) located near to HLA class II coding regions and related to antigen presentation. Therefore, polymorphisms of TAP might alter the T-cell mediated immune response and influence on the susceptibility to major depressive disorder. The aim of this study was to verify the relationship between major depressive disorder and polymorphisms of TAP2 genes.

Methods: Among the Korean patients diagnosed as major depressive disorder by DSM-IV, 112 patients without neurological illness, hormonal disorder, or comorbid mental illness were selected. Blood was obtained from 184 age-and sex-matched control subjects with no history of autoimmune and psychiatric disease. TAP2 polymorphic residues at positions 379, 565, and 665 in the TAP2 gene were found using amplification refractory mutation system-polymerase chain reaction (ARMS-PCR). The resulted products, TAP2^379, TAP2^565, TAP2^665 were assessed.

Results: Distribution of the alleles in patients with major depressive disorder was not significantly different from those of control.

Conclusions: In conclusion, these results suggest that the polymorphisms in TAP2 gene are not involved in the pathophysiology of major depressive disorder in the Korean population.

References:

NR334  Tuesday, May 4, 12:00 p.m.-2:00 p.m.
Time to Onset of Clinical Response and Psychosocial Functioning in Depression

George I. Papakostas, M.D., Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC 812, Boston, MA 02114; Timothy J. Petersen, Ph.D., Eliana Tossani, Ph.D., Andrew A. Nierenberg, M.D., Jonathan E. Alpert, M.D., Maurizio Fava, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize the relationship between time to onset of clinical response and psychosocial functioning in major depression.

Summary:
Background: Major depressive disorder (MDD) is associated with significant disability, having a profound impact on psychosocial functioning. While the successful treatment of depression is often accompanied by an improvement in psychosocial functioning, it remains to be determined whether a quicker onset of response results in better psychosocial functioning in responders.

Methods: 128 MDD outpatients who responded to an eight-week, 20-mg trial of fluoxetine completed the Social Adjustment Scale (SAS-SR) at baseline and week 8. Onset of response was defined as a 30% or greater reduction in HAM-D-17 scores compared with baseline. A multiple regression was used to test whether time to onset of response predicted overall SAS-SR scores at week 8, controlling for overall overall SAS-SR scores at baseline.

Results: There was a significant negative relationship between time to onset of response and the overall SAS-SR score at week 8, controlling for the overall SAS-SR score at baseline (p=0.044).

Conclusions: This is the first study to demonstrate an earlier onset of clinical response to result in better psychosocial function-
NR335 Tuesday, May 4, 12:00 p.m.–2:00 p.m.  
QTc Interval During Ziprasidone Treatment of Patients With Schizophrenia  
Supported by Pfizer Inc.  
Wilhelm Haverkamp, M.D., Department of Cardiology, University Charlie, Augustenburger Platz 1, Berlin 13353, Germany; Dieter Naber, M.D., Wolfgang Maier, Siegfried Kasper, M.D., Eva-Maria Woll, M.D.  

Educational Objectives:  
At the conclusion of this session, the participant should be able to judge the cardiovascular safety profile of Ziprasidone treatment.  

Summary:  
In placebo-controlled studies, ziprasidone modestly prolonged the QTc interval. The aim of this study was to evaluate the electrocardiographic effects and cardiac safety of ziprasidone.  

Methods: ZEISIG was a prospective, multicenter, open study evaluating ziprasidone (80–160 mg/day) in patients with schizophrenia and related psychosis. ECG recording were obtained before ziprasidone, after seven days and 12 weeks.  

Results: 739 ECGs from 271 pts. (mean age 37 ± 10 years, 160 males (59%)) were analyzed. After 12 weeks, intention-to-treat analysis revealed slight prolongation of rate-corrected QTc interval (Bazett) from 391.9 ± 23.6 ms (baseline) to 400.00 ± 21.3 ms (mean QTc prolongation 8.1 ms). QTc values above ≥ 470 ms were not observed. Three pts. (1.1%) had QTc increases ≥ 60ms, accompanied by increased heart rate. Significant prolongation of QTc was only observed in patients with baseline QTc < 400 ms. No significant changes were measured when baseline QTc exceeded 400 ms. In none of the pts., ziprasidone had to be discontinued due to cardiac side effects.  

Conclusion: Only slight prolongation of the corrected-Q-T interval was seen with ziprasidone. Neither torsade de pointes nor severe arrhythmias were observed. The results suggest that ziprasidone therapeutically administered to pts. with schizophrenia and related psychosis, is a safe treatment option.  

Funding Source(s): Pfizer GmbH, Germany  

References:  

NR336 Tuesday, May 4, 12:00 p.m.–2:00 p.m.  
Antidepressant Monotherapy of Bipolar Type II Major Depressive Episode  
Jay D. Amsterdam, M.D., Department of Psychiatry, University of Pennsylvania School of Medicine, 3335 Market Street, 3rd Floor, Philadelphia, PA 19104-3309; Justine Shults, Ph.D.  

Educational Objectives:  
At the conclusion of this session, the participants should have a more comprehensive understanding of treatment alternatives of BP II MDE. They will also learn about SSRI monotherapy of BP II MDE, and have a more accurate understanding of SSRI-induced manic switch episodes in BP II MDE.  

Summary:  
Background: There is a paucity of controlled data on the treatment of BP II Major Depressive Episode (MDE). Concern over manic switch episodes during antidepressant monotherapy (ADM) of BP MDE has impeded the development of effective short-term therapies. Studies by our group and others suggest that SSRIs may be a safe and effective initial therapy for BP II MDE with a low manic switch rate. In this study, we asked: 1) Is SSRI ADM an effective initial treatment of BP II MDE? and, 2) is SSRI ADM associated with a low incidence of manic symptoms?  

Method: As part of a long-term relapse-prevention study, 71 BP II MDE patients (44 women), age 19–76 years, with a HAM-D17 score ≥16 were treated with open-label fluoxetine 10–80 mg daily for up to 10 weeks. HAM-D17, CGI/S, CGI/C, and Young mania ratings (YMR) were obtained at weeks 1, 2, 4, 6, 8, and 10.  

Results: 36% of patients had a final HAM-D17 score ≥8 and 38% had a reduction in HAM-D17 baseline score ≥50% by week 10 of ADM; 37% had both a final score ≥8 and a reduction ≥50%. An ITT analysis using LOCF data showed a significant reduction in HAM-D17 score by week 6 (p<0.0005). Using generalized estimating equation (GEE) analysis, ADM-induced manic symptoms on the YMR at each study visit (vs. baseline) was not significant over time (p = 0.21).  

Conclusion: These preliminary data support earlier findings that SSRI ADM may be a safe and effective initial therapy of BP II MDE with a low manic switch rate.  

Funding Source(s): NIMH RO1 MH 060353  

References:  

NR337 Tuesday, May 4, 12:00 p.m.–2:00 p.m.  
Neurocardiac Dynamics in Clozapine-Treated Subjects With Schizophrenia  
Jong-Hoon Kim, M.D., Department of Psychiatry, Gil Medical Center, Gachon Medical School, 1198 Guwol dong Namdong gu, Incheon 405-760, South Korea; Sang-Hoon Yi, Ph.D., Yong-Min Ahn, M.D., Ung-Gu Kang, M.D., Yong-Sik Kim, M.D.  

Educational Objectives:  
At the conclusion of this session, the participant should recognize that schizophrenic patients treated with clozapine show significantly altered heart rate dynamics, and that the non-linear complexity measure of heart rate variability may be a useful tool in assessing the neuroautonomic dysfunction in schizophrenia.  

Summary:  
Introduction: The analysis of heart rate variability (HRV) has proven to be useful in evaluating the neuroautonomic dysfunctions associated with various clinical conditions. The purpose of this study was to investigate the linear and non-linear dynamic measures of HRV, and to evaluate their relationship with the psychotic symptom severity, in clozapine-treated schizophrenic subjects.  

NR338 Tuesday, May 4, 12:00 p.m.–2:00 p.m.  
Assessing the Neuroautonomic Dysfunction in Schizophrenia  
Jong-Hoon Kim, M.D., Department of Psychiatry, Gil Medical Center, Gachon Medical School, 1198 Guwol dong Namdong gu, Incheon 405-760, South Korea; Sang-Hoon Yi, Ph.D., Yong-Min Ahn, M.D., Ung-Gu Kang, M.D., Yong-Sik Kim, M.D.  

Educational Objectives:  
At the conclusion of this session, the participant should recognize that schizophrenic patients treated with clozapine show significantly altered heart rate dynamics, and that the non-linear complexity measure of heart rate variability may be a useful tool in assessing the neuroautonomic dysfunction in schizophrenia.  

Summary:  
Introduction: The analysis of heart rate variability (HRV) has proven to be useful in evaluating the neuroautonomic dysfunctions associated with various clinical conditions. The purpose of this study was to investigate the linear and non-linear dynamic measures of HRV, and to evaluate their relationship with the psychotic symptom severity, in clozapine-treated schizophrenic subjects.  

NR339 Tuesday, May 4, 12:00 p.m.–2:00 p.m.  
The Neuroautonomic Dysfunction in Schizophrenia  
Jong-Hoon Kim, M.D., Department of Psychiatry, Gil Medical Center, Gachon Medical School, 1198 Guwol dong Namdong gu, Incheon 405-760, South Korea; Sang-Hoon Yi, Ph.D., Yong-Min Ahn, M.D., Ung-Gu Kang, M.D., Yong-Sik Kim, M.D.  

Educational Objectives:  
At the conclusion of this session, the participant should recognize that schizophrenic patients treated with clozapine show significantly altered heart rate dynamics, and that the non-linear complexity measure of heart rate variability may be a useful tool in assessing the neuroautonomic dysfunction in schizophrenia.  

Summary:  
Introduction: The analysis of heart rate variability (HRV) has proven to be useful in evaluating the neuroautonomic dysfunctions associated with various clinical conditions. The purpose of this study was to investigate the linear and non-linear dynamic measures of HRV, and to evaluate their relationship with the psychotic symptom severity, in clozapine-treated schizophrenic subjects.
Methods: Fifty schizophrenic patients treated with clozapine as monotherapy and 50 age- and sex-matched normal controls were evaluated for HRV analysis. HRV measurements were obtained from a 30-minute resting electrocardiogram. The linear and novel non-linear analyses of HRV were performed. The severity of psychotic symptoms was assessed using the Positive and Negative Syndrome Scale (PANSS).

Results: In the patient group, the complexity measures as well as the time and frequency domain measures of HRV were significantly lower than in the control group (p<0.001). The PANSS total and positive symptom subscale scores had significant negative correlations with the sample entropy (SampEn) value, after adjustment for the effect of clozapine dose (p<0.01).

Conclusions: The schizophrenic patients treated with clozapine had markedly different heart rate dynamics compared to normal controls. The severity of psychotic symptoms was associated with the SampEn value, suggesting that the non-linear complexity measure might be useful in assessing the neuroautonomic dysfunction in schizophrenia.

References:

NR338 Tuesday, May 4, 12:00 p.m.—2:00 p.m.
Incidence of Metabolic Syndrome in Olanzapine and Aripiprazole Patients
Daniel E. Casey, M.D., P3 MireCC, Portland VA Medical Center, 3710 SW, U.S. Veterans Hospital Road, Portland, OR 97239; Gilbert J. L’italien, Ph.D., Paul Cislo

Educational Objectives:
At the conclusion of this presentation, the participant should be able to understand the relevance of metabolic syndrome risk factors and the development of new-onset diabetes and cardiovascular disease.

Summary:
Objective: Metabolic syndrome (Met-S) is a strong determinant of new onset diabetes and myocardial infarction. We compared the incidence or worsening of Met-S among patients from pooled clinical trials.

Methods: Met-S was defined by presence or exacerbation of 3/5 risk factors: obesity was defined as relevant weight gain (>5%, BMI >25 kg/m²); hypertriglyceridemia (15% increase, >150 mg/dl); low HDL (15% decrease, <40 mg/dl); hypertension (>8 mmHg increase, DBP >85 mmHg or >12 mmHg increase, SBP >135 mmHg); and elevated glucose (≥20% increase, ≥110 mg/dl). Kaplan-Meier survival curves were computed and compared by log rank test. Cox regression computed hazard ratios for Met-S incidence between olanzapine and aripiprazole.

Results: After 26 weeks of follow-up, event rates for 504 aripiprazole patients were 8.5±1.7% vs 14.4±1.9% for 505 olanzapine patients. One-year event rates were 10±1.9% for aripiprazole patients vs 20.0±2.3% for olanzapine patients. The relative risk for Met-S was doubled for olanzapine patients vs aripiprazole patients (RR=2.1; 95% CI: 1.3–3.1; p=0.0016).

Conclusion: Onset and worsening of clinically relevant Met-S is substantially greater for olanzapine patients than aripiprazole patients. The association between Met-S and diabetes and cardiovascular disease dictates careful consideration of antipsychotic choices for at-risk patients.

References:

NR339 Tuesday, May 4, 12:00 p.m.—2:00 p.m.
Safety of Intramuscular Olanzapine in Comorbidly Ill, Acutely Agitated Patients With Dementia Supported by Eli Lilly and Company
John P. Houston, M.D., Department of Neuroscience, Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285; Christopher Kaiser, Ph.D., Vicki P. Hoffmann, Pharm.D., Jonna Ahi, Ph.D., Donald P. Hay, M.D., Paula T. Trzepacz, M.D.

Educational Objectives:
At the conclusion of this session, participants should be able to demonstrate the safety of intramuscular olanzapine in treating acute agitation in patients with Alzheimer’s disease (AD) or mixed/vascular dementia (MVD) who also had critical medical comorbidities.

Summary:
Objective: To examine the safety of intramuscular (IM) olanzapine (OLZ) in treating acute agitation in patients with Alzheimer’s disease (AD) or mixed/vascular dementia (MVD) who also had critical medical comorbidities.

Methods: Post hoc analysis of a double-blind, randomized study comparing treatment-emergent adverse events (TEAE) among dementia patients (N=272) with major comorbid medical conditions, who were received IM OLZ 5.0 mg, IM OLZ 2.5 mg, IM lorazepam (LZP) 1.0 mg, or IM placebo (PBO) over a 24-hour period.

Results: Patients characteristics: 77.6 years old, 61% female, 40% MVD and 60% AD. Baseline comorbid conditions included: hypertension 40.1%, cardiac disorder 37.1%, chronic obstructive pulmonary disease 9.9%, diabetes 10.6%, and hypothyroidism 13.6%. No specific TEAE was more common in any active treatment group than PBO overall or for any subgroup (dementia type or cardiac comorbidity). Total TEAE were greater in patients treated with IM 5.0 mg OLZ than IM PBO in two subgroups (MVD, p=0.023, and cardiac disorder, p=0.008).

Conclusions: In this 24-hour study, treatment of acute agitation with IM OLZ 2.5 mg, IM OLZ 5.0 mg, or IM LZP 1.0 mg was well tolerated among elderly patients with dementia and cardiac comorbidities.

Funding Source: Eli Lilly and Company

References:
**NR340**  Tuesday, May 4, 12:00 p.m.–2:00 p.m.

**Concomitant Use of Lamotrigine and Lithium in Bipolar I Disorder**  
Supported by GlaxoSmithKline

Frederick K. Goodwin, M.D., Department of Psychiatry, George Washington University Medical Center, 2150 Pennsylvania Avenue, N.W., RM 8-435, Washington, DC 20037; Charles L. Bowden, M.D., Joseph R. Calabrese, M.D., Walter Paska, Ronald Stewart

**Educational Objectives:**

At the conclusion of this presentation, the audience will have an understanding of the safety and efficacy of concomitant use of lamotrigine and lithium.

**Summary:**

1. **Introduction:** Co-administration of lamotrigine and lithium may have important therapeutic value.

   **Objective:** To evaluate the efficacy of this combination in bipolar I disorder.

2. **Methods:** Pooled data from the preliminary phase of two maintenance trials (GW605/606) in bipolar I disorder were examined. Patients had completed an 8- to 16-week open-label phase where lamotrigine was administered as adjunctive or monotherapy. Psychiatric rating scale scores and adverse events were examined for patients who received both treatments concomitantly.

3. **Results:** 292 of 1305 (22%) patients received concomitant lamotrigine and lithium therapy, with a mean co-exposure of 8 weeks. Mean observed CGI-S and GAS scores were respectively 4.4 (SD 0.7) and 48.7 (SD 10.6) at study entry and 2.7 (SD 1.3) and 66.5 (SD 16.5) at the end of the preliminary phase. The most common adverse events were headache (23%), nausea (13%), diarrhea (10%), dizziness (10%) and infection (10%). No serious rash was reported and there was no significant difference in rash between patients who received concomitant treatment and those who did not (8% vs. 10%, p=0.43).

4. **Conclusion:** Concomitant administration of lamotrigine and lithium appeared to be effective and well tolerated in patients with bipolar I disorder.

   **Funding Source(s):** Funding for this research provided by GlaxoSmithKline

**References:**


**NR341**  Tuesday, May 4, 12:00 p.m.–2:00 p.m.

**Metabolic and Clinical Implications of Cannabis Use in Psychiatric Intensive Care**

Maria Isaac, M.D., Maudsley Trust - Gresham - PICU, Bethlem Roayl-Monas, Orchard Road, Beckenham Kent BR3 3BX, United Kingdom; Michael T. Isaac, M.D.

**Educational Objectives:**

At the conclusion of this session, the participant should be able to recognize that Cannabis abuse has metabolic implications in terms of weight gain, blood glucose and length of admission at PICU.

**Summary:**

**Background:** Cannabis may be a risk factor in adolescent psychosis. In London (UK) many psychiatric inpatients habitually use cannabis, often in large amounts. Little is currently known about the impact this makes in treatment in a psychiatric intensive care unit (PICU).

**Method:** Open-label, prospective study. One hundred and thirty nine inpatients on PICU who gave consent to the use of their data, following review by the local research ethics committee. Assessment of BPRS, TCI-240, BMI, blood glucose, cortisol, PRL, urinalysis for drugs, length of PICU admission.

**Results:** Differences among inpatients who used cannabis during admission (compared with non-users) mean weight change +10.23kg (2.25kg); number of patients still in PICU after 42 days 17/24 or 70% (19/79 or 24%); Patients that took Cannabis during admission tended to receive higher doses of drugs and remained longer in PICU. For Olanzapine, 115 versus 34.76 admission days, drug doses 30mg versus 25mg. For Risperidone, 86.43 versus 45.05 admission days; drugs doses 11mg versus 6.6mg. For Quetiapine, 95 versus 40 admissions days; drug doses 856mg versus 700mg. Inpatients who tested positive to cannabis on admission: There were statistical differences in the number of admissions 3.7 versus 2.1. There were also differences in glucose levels at admission 5.4 versus 4.6mmol/L. These differences were statistically significant.

**Funding Source(s):** The investigators are employed by the UK state National Health Service (NHS). The study has no funding from the pharmaceutical industry.

**References:**


**NR342**  Tuesday, May 4, 12:00 p.m.–2:00 p.m.

**Atypical Antipsychotics and Mood Stabilizers in Very Young Children**

Arman K. Danielyan, M.D., Cincinnati Childrens Hospital Medical Center, 3333 Burnet Avenue, Cincinnati, OH 45229; Sanjeev Pathak, M.D., Sarah Arszman, B.A., Alex Smimov, M.D., Erin Johns, B.A.

**Educational Objectives:**

At the conclusion of this session, the participants will recognize the importance of developing of the age-appropriate diagnostic criteria and medication management guidelines for very young children with psychiatric problems.

**Summary:**

**Background:** DSM-IV criteria for mood disorders are not easily applied in very young children (the ages 3–6 years). Use of atypical antipsychotics (AA) and mood stabilizers (MS) for the treatment of particular psychiatric diagnoses in this age group is also understudied.

**Objective:** To study practice patterns for the prescription of AA and MS and the correlation of AA and MS with specific DSM-IV diagnoses in very young hospitalized children.

**Methods:** We conducted a retrospective chart review of 93 children, who were admitted to a psychiatric inpatient unit and were less than 7 years old (6.5 + 13 months).

**Results:** AA and MS were prescribed in a variety of diagnoses. Of the 45 patients receiving AA, 33 were diagnosed with mood disorder (73.3%), with prevailing diagnosis of BPD NOS (n=12). Of 19 patients on a MS, mood disorder were diagnosed in 15 patients (78.9%) with the most common diagnoses BPD NOS (n=11).

**Conclusions:** AA and MS are commonly prescribed for very young children based on their behavioral symptoms rather than...
on the DSM-IV diagnoses. Further studies on phenomenology and diagnostic criteria of pediatric psychiatric disorders are needed. Controlled trials on the use of psychotropics for particular psychiatric diagnoses in this age group are also necessary.

References:

NR343 Tuesday, May 4, 12:00 p.m.–2:00 p.m.
Treatment of Delirium and Dopamine Transporter-Gene Polymorphisms
Chang-Su Han, M.D., Department of Psychiatry, Korea University, 516, Gojan-Dong, Ansan City 425-020, South Korea; Jee-Yeon Kim, M.D., Yong-Ku Kim, M.D., Soyoung I. Lee, M.D., In-Kwa Jung, M.D.

Educational Objectives:
At the conclusion of this session, the participant should know the relationship of response to antipsychotics of delirium and dopamine transporter gene polymorphisms.

Summary:
Objectives: Delirium is a common disorder in general hospital that is characterized by disturbances of consciousness. Relatively small doses of antipsychotic drugs are used in the treatment of delirium. We will investigate the useful dosages of haloperidol and risperidone in the treatment of delirium and relationships of the treatment response, response time, treatment doses and dopamine transporter gene polymorphisms.
Method: Either haloperidol or risperidone were administered to the delirium patients. Changes of delirium symptoms were measured in a daily basis until remission. Genetic polymorphisms of dopamine transporter were determined.
Results: There were no significant differences of drug response time and response rate according to dopamine transporter polymorphisms. The average treatment doses of the drugs were 1.67 ± 1.32 mg/day (haloperidol) and 1.19 ± 1.32 mg/day (risperidone). 10/10 variant of dopamine transporter gene was 35 among 10 to 24 inclusive at baseline. No concomitant psychological or physical illness were evaluated in an opened label, observational trial. Patients received a progressive crescent dosage regimen of IV mirtazapine during 14 days, starting at 6 mg during days 1 and 2, 9 mg. at days 3 and 4, and 15 mg at days 7 to 14. Efficacy was assessed using Beck Depression Inventory (BDI).

Results: The BDI score decreased from 49 points (baseline) to 24 at day 15 (statistically significant: p<0.001). All the patients showed an early improvement, defined as a reduction ≥20% of Beck score at Day 3 compared with the baseline. The acute phase of the treatment was continued with mirtazapine PO (tablets) in an outpatient modality, after seven to 15 days treatment period with IV treatment. No early dropouts were reported due to adverse events. Reported adverse events were mild and included dizziness, dizziness, dry mouth, nausea, anxiety, and orthostatic high blood pressure.

Conclusions: Mirtazapine I.V., administered gradually from 6 to 15 mg/day during seven to 14 days, was early efficacious, well tolerated, and safe for depressed inpatients with concomitant medical illness.

References:

NR345 Tuesday, May 4, 12:00 p.m.–2:00 p.m.
Divalproex Sodium Extended Release Augmentation of Donepezil
Peter M. Aupperle, M.D., Department of Psychiatry, UMDNJ, Robert Wood Johnson Medical School, 667 Hoes Lane, Piscataway, NJ 08854; Steven Sohnle, Ph.D., Julie Coleman, B.S.N., Anjali Patel, B.A., Kevin DeMarco, M.D., David Foran, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to present new data on the possible use of divalproex sodium for cognition in Alzheimer’s disease.

Summary:
Introduction: Divalproex sodium has been studied in terms of decreasing the behavioral complications in AD patients; however, no clinical data exist on the cognitive enhancing ability of Divalproex sodium, despite some positive basic science data. This protocol provides data on the use of divalproex sodium ER as an augmenting agent to donepezil for improving cognition (assessed with the ADAS-cog) in mild/moderate AD patients. Changes in behavioral complications (Neuropsychiatric Inventory) were also examined.
Methods: Subjects were enrolled if they had a diagnosis of AD and had a Mini-Mental Status Examination (MMSE) score within the range of 10 to 24 inclusive at baseline. No concomitant psy-
NR346 Tuesday, May 4, 12:00 p.m.—2:00 p.m.
Tolerability and Efficacy of Divalproex Extended Release in Psychiatric Patients
Supported by Abbott Laboratories
Richard S. Jackson, M.D., Neurobehavioral Med, E4111 Andover Road, Suite 220, Bloomfield Hills, MI 48302; Sanjeev Venkataraman, M.D., Mark Owens, D.O., Richard B. Atkins, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize that Divalproex DR is FDA approved for acute mania and that Divalproex (ER) is a once-daily preparation of Divalproex not approved for bipolar disorder. Patients’ stable on Divalproex DR were able to switch to ER without loss of efficacy or side effects. Once daily dosing may increase compliance.

Summary:
Introduction: Divalproex Delayed-Release (DR) is FDA-approved for acute mania. Divalproex Extended-Release (ER) is a sustained-release formulation intended for chronic daily dosing.
Objective: To assess the tolerability and effectiveness of ER in patients.
Methods: The design was a 12- to 24-week, open prospective investigation of 52 patients previously stabilized on DR, who were abruptly switched to a comparable daily dose of ER. Patients were seen monthly. Clinical status was assessed using the Young Mania Rating Scale (YMRS), Hamilton Depression Rating Scale (Ham-D), and a side-effect profile. Pertinent serial laboratory tests were obtained.
Results: Patients tolerated the single daily dose of ER well with no increase in side effects. No significant changes in laboratory tests or twelve-hour valproate blood levels occurred. Patients maintained clinical stability after switching to the ER formulation as evidenced by a statistically significant decrease in baseline to endpoint scores on the YMRS and HAM-D. We speculate this represents increased compliance with ER.
Conclusions: Psychiatric patients previously maintained on multiple daily doses of DR were able to tolerate and maintain clinical stability after an immediate switch to chronic daily dosing of Divalproex ER.
Finding Source: Abbott-Labs.

References:

NR347 Tuesday, May 4, 12:00 p.m.—2:00 p.m.
Pretreatment Suicidality as a Predictor of Response to Fluoxetine
Jessica L. Murakami, B.A., Psychiatry Department, Mass. General Hospital, 50 Staniford Street, #401, Boston, MA 02114; Dan V. Iosifescu, M.D., Paolo Cassano, M.D., Jonathan E. Alpert, M.D., Andrew A. Nierenberg, M.D., Maurizio Fava, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize suicidality as a predictor of poorer response to fluoxetine in subjects with major depression.

Summary:
Background: Despite select reports of fluoxetine-induced suicidality, studies suggest that fluoxetine is not associated with an increased risk of suicidal acts or thoughts among depressed patients (Beasley et al. 1992). Studies also indicate that improvement in suicidal ideation is greater with fluoxetine than with placebo (Tollefson et al. 1993) and improves relatively early during treatment (Worthington et al. 1995). However, it is unclear whether or not pretreatment suicidality is a predictor of response to fluoxetine. We assessed the impact of pretreatment suicidality as defined by the third item of the Hamilton Depression Rating Scale (HAM-D-17) on antidepressant response to fluoxetine among outpatients with major depressive disorder (MDD).

Method: Outpatients aged 18–65 (n=356) with MDD (SCID-DSM-III-R criteria), who received open-label fluoxetine (20 mg/day) for eight weeks were assessed using the 17-item Hamilton Depression Rating Scale (HAM-D-17).

Results: Gender, age, age of onset, duration of current depressive episode, and number of episodes did not predict response to fluoxetine using linear regression. Greater severity of depression lower percent change of HAM-D-17 score (p<.001), as did the Hamilton Item #3 (p<.03). Controlling for initial severity, suicidality continued to predict lower percentage change of HAM-D-17 score after eight weeks of active treatment (p<.05).

Conclusion: The results of this study suggest that pretreatment suicidality significantly predicts poorer response to fluoxetine among outpatients with MDD. Future research should test whether more aggressive dosing could overcome this effect and whether or not this latter holds true for other antidepressant treatments.

Funding Source(s): NIMH grant ROI-MH48483

References:
Low Incidence of Lamotrigine Treatment-Emergent Rash With Dermatology Precautions
Supported by GlaxoSmithKline

Po W. Wang, M.D., Department of Psychiatry, Stanford University, 401 Quarry Road, Room 2124, Stanford, CA 94305; Rebecca A. Chandler, B.S.; Andrea M. Alarcon, B.A.; Cecylia Nowakowska, M.D., Wendy K. Marsh, M.D., Terence A. Ketter, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize that dermatology precautions (limiting antigen exposure) during the first three months of treatment with lamotrigine may yield a low incidence of rash.

Summary:

Objective: To assess treatment-emergent rash incidence when using dermatology precautions (limited antigen exposure) during lamotrigine initiation.
Method: In a retrospective chart review, we assessed rash incidence in 100 bipolar disorder patients instructed for the first three months on lamotrigine, to NOT ingest other new medicines or new foods, or utilize new cosmetics, conditioners, deodorants, detergents, or fabric softeners, and to avoid sunburn or poison ivy/oak exposure. Lamotrigine was not started within two weeks of having a rash, viral syndrome, or vaccination.
Results: No patient had serious rash. Benign rash occurred in 6/100 (6%), but three of these patients were not adherent to dosage recommendations or dermatology precautions. Among the remaining patients, 3/97 (3.1%) had benign rash, with 2/97 (2.1%) considered related to lamotrigine. Only 3/100 (3%) discontinued lamotrigine due to benign rash, including one nonadherent patient with rash unrelated to lamotrigine who was subsequently uneventfully rechallenged while adhering to dermatology precautions and dosage recommendations.
Conclusion: 3.1% of patients adhering to dermatology precautions and dosage recommendations developed treatment-emergent rash, lower than the 10% incidence in other clinical studies. Systematic studies are needed to confirm these preliminary findings suggesting that dermatology precautions may yield a low incidence of rash with lamotrigine.

Funding Source(s): GlaxoSmithKline

References:

NR349 Tuesday May 4, 12:00 p.m.–2:00 p.m.
Relationship of Antipsychotics to New Cases of Diabetes Mellitus
Supported by Eli Lilly and Company, Janssen Research and Pfizer, Inc.

Leslie L. Citrome, M.D., Nathan Kline Institute, 140 Old Orangeburg Road, Building 37, Orangeburg, NY 10962; Ari B. Jaffe, M.D., Jerome Levine, M.D., Baerbel Allingham, M.S., James Robinson, M.S.

Educational Objectives:
At the conclusion of this session, the participant should recognize that second-generation antipsychotics may increase the risk of developing diabetes mellitus compared with exposure to first-generation antipsychotics.

Summary:

Objective: To describe the extent of use of mood stabilizers (lithium and anti-epileptic agents) among hospitalized psychiatric patients with schizophrenia.
Method: A database containing patient information and drug prescription information for every inpatient within the adult civil facilities of the New York State Office of Mental Health (NYSOMH) was queried for the period 1994 through 2002.
Results: Mood stabilizer use among NYSOMH inpatients (N=21,132 in 1994 and N=9,237 in 2002) has steadily increased from 36.5% in 1994 to 60.8% in 2002. For patients diagnosed with schizophrenia the increase has been from 26.2% in 1994 to 47.6% in 2002. Valproate is the most commonly used mood stabilizer, with 35.4% of all NYSOMH patients with schizophrenia receiving valproate in 2002. Although use is adjunctive to antipsychotics, dosage and duration of use are substantial, with patients with schizophrenia receiving valproate for an average of 81.9% of their hospital stay, at an average daily dose of 1628 mg. In comparison, among patients with schizophrenia hospitalized in 2002, the percent use of lithium, carbamazepine, gabapentin, lamotrigine, topiramate, and oxcarbazepine were 8.7%, 1.9%, 8.6%, 1.2%, 3.1%, and 3.6%, respectively.

Conclusions: With the exception of lithium, valproate (in the divalproex sodium preparation), and lamotrigine, none of the reported mood stabilizers have US Food and Drug Administration approval for a psychiatric disorder, and none have approval for the treatment of schizophrenia. Nevertheless, lithium and antiepileptic agents are commonly used as adjunctive agents for the treatment of schizophrenia. Definitive double-blind randomized efficacy studies are desirable to place these agents into clinical perspective.

Funding Source(s): ABBOTT

References:

NR351 Tuesday, May 4, 12:00 p.m.—2:00 p.m.
Switching From Standard Divalproex to Extended Release in Schizophrenia
Supported by Abbott Laboratories
Leslie L. Citrome, M.D., Nathan Kline Institute, 140 Old Orangeburg Road, Building 37, Orangeburg, NY 10962; Fabien Tremeau, M.D., Pe Shein Wynn, M.D., Biman Roy, M.D., Hassan Dinakar, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize treatment patterns in patients diagnosed with bipolar depression in managed care organizations.

Summary:
Objective: To examine managed-care prescribing patterns for patients beginning pharmacologic treatment in the depressive phase of bipolar.

Methods: This retrospective study (1995–2002) included a cohort of 1,203 patients who had three consecutive years of data, received an ICD coded diagnosis of bipolar depression and received one of four classes of psychotropic medication (i.e., antidepressant, antipsychotic, benzodiazepine, or mood stabilizer). Treatment patterns were observed for a one-year period post diagnosis.

Results: 77% of extracted data were between 1999–2002. 55 different medications were used to create multiple unique mono and/or combination pharmacologic treatments. 9% of patients began their treatment in accordance with APA guidelines, whereas, 16% began treatment using only an antidepressant. As switches in treatment occur, use of mono-therapy treatments decrease (-12%) and use of four or more medication combinations increase (+9%). One third of patients were treated with four or more medications in combination, at some point, during the year following diagnosis.

Conclusion: Pharmacologic treatment of bipolar depression is characterized by polypharmacy, reflecting the complexity of the disorder; and is often not aligned with guidelines. There is a need to study how these patterns impact service utilization and costs, as well as to further understand the treatment patterns.

Funding Source(s): Funded by Eli Lilly and Company

References:
NR353  Tuesday, May 4, 12:00 p.m.–2:00 p.m.
Trend in Use of SSRI Antidepressants for Children With Depression
David A. Sclar, Ph.D., Department of Pharmacy, Washington State University, PO Box 646510, Pullman, WA 99164–6510, Thea R. Moore, Pharm. D., David A. Moore, Ph.D., Tracy L. Skaer, Linda M. Robison, M.S.P.H.

Educational Objectives:
At the conclusion of this session, the participant should: (1) recognize the upward trend in the prescribing of selective serotonin reuptake inhibitors (SSRIs) to treat depression in children and adolescents 5–18 years old for the time period 1990 through 2001; and (2) recognize the changes in the types of SSRIs being prescribed to treat the depression over this time period.

Summary:
Objective: The American Academy of Child and Adolescent Psychiatry advocates the use of selective serotonin reuptake inhibitors (SSRIs) as first-line pharmacotherapy in the treatment of depression in children and adolescents due to the enhanced safety profile as compared with that of tricyclic antidepressants. This study was designed to discern trends in the prescribing of SSRIs overall and by type, for the treatment of depression in children and adolescents 5–18 years old.

Methods: Using data from the National Ambulatory Medical Care Survey, office-based physician visits resulting in a diagnosis of depression (ICD-9-CM codes 296.2 - 296.36; 300.4; or 311) were extracted and the prescribing of SSRIs by type (fluoxetine, paroxetine, sertraline, citalopram) was discerned for the years 1990–2001. Trend analysis was conducted using three time intervals: 1990–93; 1994–97; 1998–01.

Results: Over the time-frame examined, the percent of patients prescribed an SSRI increased from 20.7% to 39.7%. By 2001, children and adolescents in receipt of an SSRI (n=633, 059) were prescribed fluoxetine (12%) paroxetine (7.7%), sertraline (8.6%), and citalopram (7.1%).

Conclusion: These data reveal significant growth in the prescribing of SSRIs to children and adolescents, with fluoxetine the most widely prescribed.

Funding Source(s): 2001 Independent Investigator Award. National Alliance for Research on Schizophrenia and Depression

References:

Summary:
Rationale: antidepressants are usually prescribed for the treatment of both depression and anxiety disorders. Preclinical studies results trying to decipher the pharmacological mechanism of this dual action are inconsistent.

Objectives: the purpose of this study was to investigate the effect of an acute administration of antidepressants (serotonergic and noradrenergic compounds) in rats submitted to the elevated plus-maze.

Methods: fluoxetine (FL) (2.5, 5, 10, 15 mg/kg Intra-Peritoneally-IP), paroxetine (PA) (0.1, 3, 12 mg/kg IP), desipramine (DE) (2.5, 5, 10 mg/kg IP) or their vehicles (VE) were investigated 30 minutes following an acute administration.

Results: compared with control FL (5 and 10 mg/kg) and PA (3 and 12 mg/kg) decreased the percentage of time spent in the open arms (FL: 11% and 11% vs 19%, PA: 16% and 12% vs 24%), FL (5, 10 and 15 mg/kg) and PA (3 and 12 mg/kg) decreased the percent of inactive time (FL: 10%, 9% and 10% vs 19%, PA: 14% and 14% vs 24%). DE was inactive on this paradigm. These observed effects were not due to motor activity changes. Significant differences were also observed in the distance covered as well as in the spatial sharing of the activity in the maze.

Conclusions: the elevated plus-maze shows a good sensitivity for detecting anxiogenic effects of serotonergic drugs. Acute treatment only with FL and PA produced an anxiogenic profile. Thus, the pharmacological mechanism appears to be due more to serotonergic than adrenergic compounds and constitute a strong argument in favour of a serotoninergic system dysfunctioning in the pathophysiology of anxiety.

References:

NR354  Tuesday, May 4, 12:00 p.m.–2:00 p.m.
Anxiogenic-Like Effect of Acute Fluoxetine, Paroxetine, and Desipramine on Rats Tested on the Elevated Plus-Maze
Dominique Drapier, M.D., Hospital G. Regnier, 108 Avenue Gal Leclerc, Rennes 35000, France; Daniele Bentue-Ferrer, Ph.D., Herve Allain, M.D., Bruno Millet, M.D., Jean M. Reymann, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to demonstrate that an acute administration of serotonergic compound on rats produces an anxiogenic effect that is not found with noradrenergic compounds.

Summary:
Objective: To evaluate optimal initial dosing of ziprasidone in patients with acute exacerbation of schizophrenia or schizoaffective disorder.

Methods: We analyzed ziprasidone’s clinical trial database for efficacy and tolerability data respecting two initial dosages, 40 or 80 mg/d. Pooled data from seven fixed- and flexible-dose studies (N=2174) were analyzed for initial and overall efficacy, initial and total discontinuations, and adjunctive medications.

Results: Overall, subjects initiating ziprasidone at 80 mg/d demonstrated improved outcomes compared with subjects initiating therapy at 40 mg/d. Improved efficacy was indicated by greater
reductions in BPRS Total scores at week 1 and endpoint, and significantly lower rates of discontinuation from lack of efficacy at week 1 (1.3% vs 4.1%, respectively; P<0.05) or any time (19.2% vs 26.6%, respectively; P<0.05). Subjects initiating at 80 mg/d were less likely to require adjunctive lorazepam than those initiating at 40 mg/d. There were no between-group differences in discontinuations due to AEs or type and frequency of AEs. Mean doses of ziprasidone in the flexible-dose trials ranged from 120–160 mg/d.

Conclusions: Initiating ziprasidone at 80 mg/d and reaching minimum target goals of 120 mg/d are associated with improved overall outcomes compared with lower dosages. Higher initial dosing is well tolerated.

Funding Source(s): Supported by funding from Pfizer Inc.

References:

NR356 Tuesday, May 4, 12:00 p.m.–2:00 p.m.
Factor Analysis of Onset of Therapeutic Effect of Mirtazapine Versus SSRIs
Albert J. Schutte, M.D., Organon Inc., 56 Livingston Avenue, Roseland, NJ 07068; Silvia Van Der Flier, Ph.D., Anja J. Heukels

Educational Objectives:
At the conclusion of this session, the participant should be able to: (1) describe the design and methods of this meta-analysis comparing mirtazapine and SSRIs; (2) discuss the results of this pooled analysis and its implications for the clinical use of mirtazapine or SSRIs with respect to onset of therapeutic effects.

Summary:
It is of relevance to identify an antidepressant that provides a fast onset of therapeutic action. A meta-analysis using individual patient data from 11 double-blind, randomized, controlled studies of mirtazapine versus SSRIs was performed to compare the efficacy and onset of action of mirtazapine with that of SSRIs based on HAMD-17 Total scores, HAMD Factor I (anxiety/somatization), V (retardation), and VI (sleep disturbances) and the Bech Depression Factor. Statistical analysis was performed based on the Intent-To-Treat groups (n=1266; n=1272). A statistically significant advantage in the mean change in total HAMD score from baseline (p<0.05) in favor of mirtazapine was shown. The difference in responder rates were statistically significant and in favor of mirtazapine at all assessments. The difference in the change from baseline on the HAMD Bech depression factor was in favor of mirtazapine at all assessments, being statistically significant at Week 2 (p<0.05). A statistically significant difference in favor of mirtazapine was shown for Factor I at Weeks 1, 2 and 4 of treatment and for Factor V and VI at all assessments (p<0.05). These results sustain the previously retrospectively observed faster onset of therapeutic action with mirtazapine compared with SSRIs treatment and the anxiolytic and sleep improving properties of mirtazapine.

References:

NR357 Tuesday, May 4, 12:00 p.m.–2:00 p.m.
Combining Two Antidepressants From Treatment Start: A Preliminary Analysis
Supported by Organon Inc.
Pierre Blier, M.D., Department of Psychiatry, University of Florida, 100 Newell Drive, Suite L4100, Gainesville, FL 32608; Herbert E. Ward, M.D., William Jacobs, M.D., Chantal Herbert, R.N., Shella A. O’Hara, R.N., Teresa A. Pigott, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize that combining two antidepressants with complementary mechanisms of action are: (1) safe to use from treatment initiation; (2) well tolerated; and (3) that with some combinations a more robust antidepressant action may be obtained within a standard six-week period.

Summary:
Introduction: Remission rates using adequate doses of single antidepressant drugs given for a sufficient time are generally below 50%, implying that in more than half the patients, additional therapeutic measures have to be taken. A common strategy consists in adding a second agent with a different mechanism of action on the serotonin or the norepinephrine system. Methods: In this 6-week double-blind study, mirtazapine (30 mg HS) was combined with fluoxetine (20 mg/day), venlafaxine (75 mg/day titrated to 225 mg/day in two weeks), or bupropion (150 mg/day) from treatment initiation. Fluoxetine alone was used as a control. Results: Preliminary analysis of the first 56 randomized patients showed that the combinations produced a significant improvement starting at day 4, but only at day 10 in the fluoxetine group using the Montgomery Asberg Depression Rating Scale (MADRS). The venlafaxine+mirtazapine group had the most robust improvement separating from the fluoxetine group by seven points on the MADRS in the last three weeks, as well as on a Symptom Check List (13 symptoms) filled by the patients. Conclusion: These preliminary results suggest that mirtazapine combinations are well tolerated (<10% dropouts), may exert rapid symptom reduction, and that venlafaxine+mirtazapine appears to be a superior strategy.

References:

NR358 Tuesday, May 4, 12:00 p.m.–2:00 p.m.
Adjunctive Ziprasidone in Bipolar Mania: Short-Term and Long-Term Data
Supported by Pfizer Inc.
Richard H. Weisler, M.D., Department of Psychiatry, UNC Chapel Hill/Duke, 700 Spring Forrest Road, Suite 125, Durham,
Objective: To evaluate efficacy/tolerability of ziprasidone plus lithium in acute bipolar mania and long-term treatment of bipolar disorder.

Methods: Lithium-treated bipolar inpatients with Mania Rating Scale (MRS) score ≥14 were randomized to ziprasidone (80–160 mg/d) or placebo for 21 days (lithium serum levels: 0.8–1.2 mEq/L). Between-group differences and LS change scores were compared. Patients could enter a 104-week, open-label continuation study (ziprasidone 40–160 mg/d).

Results: Day 4 rate of change was significant with ziprasidone (n=102) but not placebo (n=103) for MRS, CGI-S, CGI-I, Behavior and Ideation, and Ham-D. Day 14 rate of change in MRS and CGI-S (primary endpoints) was comparable, but mean changes with ziprasidone were significantly greater for all PANSS variables at Days 14 and 21. Improvement from continuation baseline stabilized at Weeks 4–12 for MRS, at Weeks 12–28 for CGI-S, and after Week 52 for PANSS Positive. MRS and PANSS Positive improvements were sustained to endpoint (LOCF); PANSS Total improvement, until Week 28 (fluctuations thereafter). Ziprasidone was well tolerated.

Conclusions: Ziprasidone plus lithium effected significantly greater Day 4 rate of change in mania-related psychopathology, suggesting more rapid efficacy than with lithium alone. Long-term improvements were sustained, with good tolerability.

Funding Source(s): Pfizer

References:

NR359  Tuesday, May 4, 12:00 p.m.—2:00 p.m.
Carbamazepine Extended Release Treatment of Manic and Mixed Symptoms
Supported by Shire Pharmaceutical Development, Inc.
Richard H. Weisler, M.D., Department of Psychiatry, UNC Chapel Hill/Duke, 700 Spring Forrest Road, Suite 125, Durham, NC 27609; Amir H. Kalali, M.D., Terence A. Ketter, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to discuss the acute efficacy and safety of extended-release carbamazepine in the treatment of manic and mixed patients with bipolar disorder.

Summary:
Objective: To evaluate the acute efficacy and safety of extended-release carbamazepine capsules (ERC-CBZ; SPD417) in the treatment of manic and mixed symptoms in patients with bipolar disorder.

Method: A 3-week, randomized, double-blind, placebo-controlled, parallel-group study was conducted at 27 sites. 204 subjects (mean age 38 years; 47.5% female; 53% mixed) with a DSM-IV diagnosis of Bipolar Disorder (manic or mixed) were randomized to placebo or ERC-CBZ (initiated at 200 mg bid and increased to a maximum daily dosage of 1600 mg). Efficacy was assessed by the Young Mania Rating Scale (YMRS), the Clinical Global Impression Scale (CGI), and Hamilton Depression Rating Scale (HDRS).

Conclusions: ERC-CBZ was found to be effective for the treatment of manic and mixed symptoms in bipolar patients for up to 21 days at a titrated dose of between 200 mg and 1600 mg/d. AE s were generally mild to moderate in nature and were typical of those associated with carbamazepine.

Funding Source(s): Shire

References:

NR360  Tuesday, May 4, 12:00 p.m.—2:00 p.m.
Treatment of Manic and Mixed Patients With Carbamazepine Extended Release
Supported by Shire Pharmaceutical Development, Inc.
Richard H. Weisler, M.D., Department of Psychiatry, UNC Chapel Hill/Duke, 700 Spring Forrest Road, Suite 125, Durham, NC 27609; Paul E. Keck, Jr., M.D., Alan C. Swann, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to discuss the acute efficacy and safety of extended-release carbamazepine monotherapy in the treatment of manic and mixed patients with bipolar disorder.

Summary:
Objective: Evaluate the acute efficacy and safety of extended-release carbamazepine capsules (ERC-CBZ; SPD417) as monotherapy in the treatment of manic and mixed bipolar disorder patients.

Method: A three-week, randomized, double-blind, placebo-controlled, parallel-group, multicenter study was conducted. 239 subjects (mean age 37; 30% female; 21% mixed) with a DSM-IV diagnosis of bipolar disorder (manic or mixed) were randomized to placebo or ERC-CBZ (initiated at 200 mg bid and increased by 200 mg/d if tolerated to a maximum daily dosage of 1600 mg). Efficacy was assessed by the YMRS, the CGI, and HDRS.

Results: One-hundred forty-four patients (60.2%) completed the study. There was a statistically significant difference between the treatment groups in favor of ERC-CBZ for YMRS mean total score at endpoint (P=0.0331); responders (>50% reduction in YMRS; P=0.0074); sustained responders (>50% reduction in YMRS maintained for at least 2 weeks; P=0.0024); CGI severity (P=0.0254); and CGI improvement (P=0.0007). Post-hoc analysis of mixed patients revealed improved HDRS scores in patients remaining on ERC-CBZ on day 21 (P=0.01). The most frequently reported AEs for ERC-CBZ were dizziness, nausea, and somnolence. No significant weight gain was reported.

Conclusions: ERC-CBZ was found to be effective for the treatment of manic and mixed symptoms in bipolar patients for up to 21 days at a titrated dose of between 200 mg and 1600 mg/d. AEs were generally mild to moderate in nature and were typical of those associated with carbamazepine.

Funding Source(s): Shire
References:


NR361  Tuesday, May 4, 12:00 p.m.–2:00 p.m.

Predictors of Response to a Placebo-Controlled, Double-Blind Trial of Paroxetine Controlled Release in Fibromyalgia

Supported by GlaxoSmithKline

Cynthia Purcell, M.S., Psychiatry Department, Thomas Jefferson University, 833 Chestnut Street, Suite 210E, Philadelphia, PA 19107; Ashwin A. Patkar, M.D., Prakash S. Masand, M.D., Wei Jiang, M.D., Stan Krul eviction, M.A., Eric Dube, Ph.D., Kathleen S. Peindi, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should recognize the predictors of treatment outcome in patients with fibromyalgia.

Summary:

Introduction: Many fibromyalgia patients fail to respond to pharmacological interventions. We determined whether certain clinical, behavioral and demographic variables at baseline predicted the treatment response in an ongoing double-blind trial of paroxetine controlled release (CR).

Methods: 102 patients with fibromyalgia were screened and 81 randomized to receive paroxetine CR or placebo for 12 weeks. Treatment response was defined as a 25% or greater reduction in Fibromyalgia Impact Questionnaire (FIQ) scores. A blinded logistic regression analysis was conducted to determine the baseline variables significantly predicting treatment response.

Results: Overall response was 62% with a 23% dropout rate. The subjects were 97% female, 61% Caucasian, 52% married, 57% employed with a mean age of 46 years. Current depressive disorders accounted for nearly 50% of the screen failures. About 40% of subjects had a comorbid diagnosis of Irritable Bowel Syndrome and 23% had a history of sexual or physical abuse. A significant effect of history of sexual abuse (p<.05) and a trend effect (p=0.07) of history of physical abuse on overall response was found. Severity of symptoms, personality, sleep and pain disturbances, comorbid medical and psychiatric conditions, and level of disability were not predictive of response.

Conclusion: Depression and irritable bowel syndrome appear to be common comorbid conditions in fibromyalgia. A history of sexual and physical abuse appears to predict poor response in fibromyalgia. A multivariate analysis of the data will be performed at the end of the study to examine the effect of study drug, and other clinical and demographic variables on treatment response.

Funding Source(s): GlaxoSmithKline

References:


NR362  Tuesday, May 4, 12:00 p.m.–2:00 p.m.

NMS Across the Life Span

Varadaraj R. Velamoor, M.D., Psychiatry Department, Cornell University, 28 Maplewood Lane, White Plains, NY 10605; Zachias Cernovsky, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the lack of significant relationship of age to NMS symptoms.

Summary:

Introduction/Hypotheses: We expected that symptom patterns of NMS may vary with the patient's age.

Methods: The data collected in the national NMS reporting center on 222 suspected NMS cases were analyzed: 188 (84.7%) of them met DSM-IV criteria for NMS. The data included vital signs (BP, pulse, temperature), laboratory measures (Creatine Kinase, WBC, PH, P-O2, P-CO2), and ratings of behavioral symptoms (including rigidity, dysarthria, dysphagia, agitation, coma, etc.).

Results: Statistical analyses compared 5 age groups (age 1 to 19, 20 to 34, 35 to 49, 50 to 64, and 65 to 90). There were no statistically significant differences between these 5 age groups in the respective proportions of those classified as NMS by DSM4 (x2 = 5.5, df=4, p=.05) and of those diagnosed so by Caroff's criteria (x2 = 6.1, df=4, p=.05). Further analyses involved only those who met DSM-IV criteria for NMS. No significant differences with respect to vital signs, laboratory measures, and behavioral ratings were found among the age groups except with respect to higher pulse rates in younger persons.

Conclusions/Discussion: Except for pulse, no significant age related trends in NMS diagnoses or in NMS symptom patterns were noted.

References:


NR363  Tuesday, May 4, 12:00 p.m.–2:00 p.m.

Topiramate for Acute Mania in Adolescent Patients With Bipolar I Disorder

Supported by Ortho-McNeil Pharmaceuticals

Melissa P. DelBello, M.D., Department of Psychiatry and Pediatrics, University of Cincinnati, College of Medicine, 231 Albert Sabin Way, PO Box 670599, Cincinnati, OH 45267-0599; Stuart F. Kushner, M.D., Daniel Wang, Ph.D., William Olson, Ph.D., Julie Capece, B.A., Lydia Fazzio, M.D., Norman Rosenthal, M.D.

Educational Objectives:

At the conclusion of this session, the participant should understand the role of topiramate for acute mania in children and adolescents with bipolar I disorder.

Summary:

Objective: Assess the efficacy of topiramate monotherapy in children and adolescents with acute mania.

Methods: Although designed as a 200-patient, randomized, double-blind, placebo-controlled, multicenter study of four weeks' duration, this study was terminated after randomizing 56 patients when adult mania trials failed to show efficacy. Patients were titrated to 400 mg/day. The protocol-specified primary efficacy measure was change in YMRS score from baseline to Day 28 by
Pregabalin in GAD: Does It Also Improve Core Depressive Symptoms?

Supported by Pfizer Inc.

Arifulla Khan, M.D., Psychiatry Department, Northwest Clinical Research Center, 1900 116th Avenue, N.E., Suite 112, Bellevue, WA 98004; Naomi M. Simon, M.D., Kathy J. Tobias, M.D., Jerri D. Brock, Ph.D., Gwen L. Zomberg, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to better understand subsyndromic depression in patients who have primary diagnoses of GAD and pregabalin’s safety and tolerability across its dosing range.

Summary:
Objective: Generalized anxiety disorder (GAD) is frequently complicated by subsyndromic depression. The efficacy of the novel anxiolytic pregabalin in treating subsyndromic depressive symptoms was evaluated.

Methods: Data were analyzed from all placebo-controlled studies of PGB in the treatment of DSM-IV GAD for doses from 200 to 600 mg/day to yield the analysis sample, N=1282; female=60%; mean age=39.4 yrs; base HAM-A=25.4. A Week 4/6 LOCF-endpoint analysis was performed on depressive symptom measures, including the HAM-D total score and HAM-D items 1 (depressed mood), 4–6 (insomnia factor), and 13 (somatic/pain symptoms).

Results: There was significantly greater endpoint improvement on PGB versus placebo on HAM-D total score (−5.29±0.19 versus −3.08±0.25; p<0.001), HAM-D-depressed mood (−0.21±0.03 versus −0.09±0.04; p<0.001), and HAM-D somatic/pain (−0.38±0.04 versus −0.23±0.05; p=0.02). Among patients with moderate-to-severe, middle-to-late insomnia at baseline (HAM-D items 5 and 6, score ≥3), pregabalin resulted in insomnia response (minimal-to-none) in 65% on versus 37% with placebo (p=0.01). Significant improvement was also observed with pregabalin in early insomnia.

Conclusions: Pregabalin demonstrates significant efficacy for improving depressive symptoms—such as insomnia, pain, and depressed mood—that frequently complicate the clinical presentation of GAD.

Studies funded by Pfizer.

References:
NR366  Tuesday, May 4, 12:00 p.m.–2:00 p.m.
Efficacy and Tolerability of a Direct Switch to Long-Acting Risperidone
Supported by Janssen-Cilag
Hans-Juergen Moeller, M.D., Psychiatry Department, University Munich, Nussbaumstrasse 7, Munich 80336, Germany, Andreas Schreiner, M.D., Max Schmauss, M.D., Werner K. Kissling, M.D., Dieter Naber, M.D.

Summary:
Objective: To evaluate the efficacy and tolerability of a direct switch to long-acting injectable risperidone without oral risperidone run-in.

Methods: Prospective multicenter open-label trial (SoroM). In-and outpatient patients ≥18 years with schizophrenia or other psychiatric disorders requiring long-term antipsychotic treatment, symptomatically stable and stable on their previous antipsychotic medication for ≥1 month, were enrolled. Patients were evaluated at baseline and after one, three, and six months using the Positive and Negative Syndrome Scale (PANSS), the Clinical Global Impression (CGI) and the Global Assessment of Functioning Scale (GAF).

Results: In Germany, 356 patients were enrolled (54.5% male, mean age 41.7 years). 81.5% had schizophrenia, 18.3% had schizoaffective disorder. Most patients switched from oral atypical (49.5%) or conventional depot neuroleptics (32.7%). 83.7% of the patients started on 25 mg long-acting risperidone. Mean PANSS total score decreased significantly from baseline to endpoint (72.7 to 63.1, p < 0.0001). PANSS positive and negative subscores, CGI and GAF also improved significantly (p < 0.0001 vs. baseline). No unexpected AEs occurred. 5.1% of the patients discontinued treatment prematurely due to insufficient response, 9.6% due to an adverse event.

Conclusion: Switching stable patients from various antipsychotic medications to long-acting risperidone was safe, well tolerated and associated with significant clinical improvement.

Funding Source(s): This study was supported by Janssen-Cilag.

References:

NR367  Tuesday, May 4, 12:00 p.m.–2:00 p.m.
Adjunct Modafinil Reduces SSRI-Induced Sedation in Patients With MDD
Supported by Cephalon, Inc.
Thomas L. Schwartz, M.D., Department of Psychiatry, SUNY Upstate Medical University, 750 East Adams Street, Syracuse, NY 13210; Kimberly Cole, B.A., Geoffrey M. Hopkins, M.D., Nikhil D. Nihalani, M.D., Mihai Simonescu, M.D., Nicole Jones, B.A.

Educational Objectives:
At the conclusion of this session, the participant should: (1) appreciate challenges in the management of sleepiness and fatigue associated with SSRI use; and (2) make informed decisions about modafinil as a treatment option for patients with antidepressant-induced sedation.

Summary:
Objective: Symptoms such as fatigue and sleepiness may not fully resolve in patients with major depressive disorder (MDD) treated with antidepressants (AD), and may be side effects associated with these therapies. Adjunct modafinil has been shown to reduce fatigue and improve wakefulness in patients with MDD. We evaluated adjunct modafinil in patients with MDD experiencing sedating side effects of AD.

Method: 17 patients with depressive disorder or anxiety (DSM-IV), treated with selective serotonin reuptake inhibitors (SSRIs) and reporting sedating side effects, entered a three-week, open-label study. Patients received modafinil 50-100 mg/day with flexible weekly titration. In addition to existing SSRIs. Assessments included the Epworth Sleepiness Scale (ESS). Fatigue Severity Scale (FSS). Hamilton Rating Scale for Depression (HAM-D), and Short-Form Health Survey version 2 (SF-12v2).

Results: Adjunct modafinil significantly improved wakefulness at all time points (ESS: p<0.01 vs baseline) and decreased fatigue from week 2 (ESS: p<0.01). Adjunct modafinil significantly improved mood from week 1 onwards (HAM-D total score: p<0.001).

Treatment was associated with significant improvements in health-related quality of life (HRQOL), particularly in the domains of physical and emotional health (SF-12v2 total and domain scores, p<0.05). Modafinil was well tolerated.

Conclusions: In patients with sedating side effects of SSRIs, adjunct modafinil may be efficacious in improving wakefulness, fatigue, mood, and HRQOL.

Funding Source(s): Supported by Cephalon, Inc.

References:

NR368  Tuesday, May 4, 12:00 p.m.–2:00 p.m.
The Potential for Clinically Significant Drug-Drug Interactions in Patients
Supported by Pfizer, Inc.
Sheldon H. Preskom, M.D., Dept of Psych, UKSM-W, 1010 N Kansas St, Wichita, KS 67214-3124; Rozina Shah, M.D., Seryl Silkey, Melissa Neff, Amanda Golbeck, Ph.D., Joe Choi

Educational Objectives:
Learn about the frequency of potentially clinically-significant cytochrome P450 mediated drug-drug interactions in VA patients on fluoxetine or paroxetine.

Summary:
Fluoxetine and paroxetine, at their lowest usually effective antidepressant dose, produce substantial inhibition of the drug-metabolizing enzyme, CYP 2D6 whereas sertraline does not [1].

Method: Determined the frequency of the combined use of fluoxetine/paroxetine versus sertraline with drugs principally cleared via 2D6 in VA outpatients (461 on fluoxetine/paroxetine and 435 on sertraline). Determined whether the therapeutic index and dose of the co-administered 2D6 substrate/drug posed a risk for a potentially dangerous drug-drug interaction (DDI), given substantial inhibition of 2D6.

Results: 39.7% of patients being treated with fluoxetine/paroxetine were also receiving a 2D6 model substrate/drug versus 34.2%
NR369  Tuesday, May 4, 12:00 p.m.—2:00 p.m.
Divalproex in Patients With Pervasive Developmental Disorder and Intermittent Explosive Disorder: Effectiveness as Reviewed in Medical Records of 300 Inpatients During 22 Years of Studies Supported by Abbott Laboratories
Ronald J. Hardrict, M.D., Department of Psychiatry, Quality Care Clinic, 1076 West 7th Street, St. Paul, MN 55102

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the efficacy and tolerability of Divalproex in the treatment of acute record disturbance or agitation for dually diagnosed MR/IED patients.

Summary:

Introduction: Individuals with Mental Retardation are at a greater risk of developing comorbid psychiatric illness compared to the general population. Psychopathology frequently presents as severe self-mutilation, aggression and agitation. Various psychotropic agents have been used by clinicians to reduce observed mood lability and self-injury. Many clinicians continue to use antipsychotic agents as first-line agents despite the risk of akathisia, EPS, tardive dyskinesia and neuroleptic malignant syndrome. Anticonvulsant agents have demonstrated efficacy in the treatment of Bipolar Disorder, IED, & Bipolar Spectrum disorders. If safety, tolerability and efficacy can be demonstrated in patients with Mental Retardation and Mental Illness, clinicians would have greater confidence in using these agents as first line treatments in this very challenging population.

Hypothesis: The use of Divalproex Sodium for the treatment of Intermittent Explosive Disorder in Developmentally Delayed Patients will result in improved GAF and CGI scores corresponding with symptom improvement with no increase in adverse effects, extrapyramidal effects or tardive dyskinesia.

Methods: A retrospective chart review was completed on 300 patients admitted between July 1, 2001 and July 1, 2002 to a specialized unit for the management of adults with developmental disabilities. 203 patients meeting DSM IV criteria-for-Intermittent Explosive Disorder and Mental Retardation where identified. Records of 108 patients meeting criteria and receiving treatment with Divalproex Sodium in monotherapy or adjunctive therapy were evaluated to assess patient response; safety and tolerability of treatment. GAF was measured prospectively, and CGI assessed retrospectively for each case determine treatment efficacy. A standardized adverse event scale; vital signs, weight and laboratory indices were used to assess safety and tolerability.

Results: The charts of 203 patients meeting criteria for IED/MR were evaluated. 108 patients had been treated with Divalproex Sodium. 77 of 108 patients (71%) demonstrated improved or much improved scores based on the CGI/GAF results. The most commonly observed adverse events were somnolence and mild GI disturbance. There were no reported deaths, and vital signs remained stable for all cases throughout their hospitalization.

Conclusion Discussion: Divalproex Sodium is effective for the acute management of agitation and mood lability in patients with Intermittent Explosive Disorder and Mental Retardation and should prove a valuable treatment alternative to antipsychotic agents for the treatment of this very challenging and vulnerable patient population.

Funding Source(s): Abbott Laboratories

References:


NR370  Tuesday, May 4, 12:00 p.m.—2:00 p.m.
Paroxetine Controlled Release Treatment of Irritable Bowel Syndrome Supported by GlaxoSmithKline
Prakash S. Masand, M.D., Department of Psychiatry, Duke University Medical Center, Box 3391 Duke South, Room 3050B, Yellow Zone, Durham, NC 27710; Ashwin A. Patkar, M.D., Eric Dube, Ph.D., Stan Krulewicz, M.A., Marja Mattila-Evenden, M.D., Sayed S. Alamy, M.D., Indira Varia

Educational Objectives:

At the conclusion of this session, the participant should recognize the possible role of selective serotonin uptake inhibitors in the treatment of irritable bowel syndrome.

Summary:

Introduction/Hypothesis: Irritable bowel syndrome (IBS) has a high rate of psychiatric comorbidity. Open-label studies have suggested a possible therapeutic role for selective serotonin uptake inhibitors in IBS. We examined the efficacy and safety of paroxetine-controlled release (CR) in the treatment of IBS. This is the first double-blind, placebo-controlled, randomized trial of a new generation of antidepressants in the treatment of IBS.

Methods: In an ongoing, double-blind, parallel group, prospective study followed by an open-label extension phase, 69 subjects with a diagnosis of IBS were randomized to receive paroxetine CR (dose 12.5-50 mg per day) or placebo for 12 weeks. Treatment response was defined as a 25% or greater reduction in scores on the mean composite pain scores on Interactive Voice Response System (IVRS) from randomization to end of treatment (LOCF).

Results: Preliminary analysis on 27 completed patients showed that eight of 12 (66.6%) receiving paroxetine CR and six of 15 (40%) receiving placebo were responders (chi square=1.89). The mean change in IVRS scores from randomization to end of treatment was 5.83 ± 1.32 in the placebo group (effect size=0.31). There were no serious adverse events related to either the drug or placebo.

Conclusions: The low power of the analyses did not permit demonstration of any robust treatment differences. Of note, the effect size of paroxetine CR is consistent with that observed in treatment trials of other agents in IBS.

Funding Source(s): GlaxoSmithKline
NR371 Tuesday, May 4, 12:00 p.m.–2:00 p.m.

High-Dose Ziprasidone: Efficacy and Tolerability in Clinical Practice
Supported by Pfizer Inc.

Daniel A. Deutschman, M.D., Department of Psychiatry, Southwest General, 18051 Jefferson Park Road, Suite 106, Middleburg Heights, OH 44130; Douglas Deutschman, Ph.D., John S. Chalekian, M.S.

Educational Objectives:

At the conclusion of the presentation, participants should better appreciate that treatment-resistant patients showing significant but incomplete response with ziprasidone at doses up to 200 mg/day may experience additional efficacy at doses up to 480 mg/day, without loss of safety or tolerability.

Summary:

Introduction: Ziprasidone’s clinical development program evaluated safety and tolerability at dosages ≤200 mg/d. Limited data on higher dosages are available. We review ongoing clinical experience at doses ≥480 mg/d.

Methods: Variously diagnosed patients given ziprasidone 240 mg/d met the following criteria: (1) treatment-resistant history, (2) robust but incomplete response at 160 mg/d, (3) minimal side effects. Similar criteria were applied to patients advanced stepwise to 320, 400, and 480 mg/d. An electronic medical record, Behavior2004, allowed analysis of dosages, demographics, diagnoses, efficacy, and AEs.

Results: A total of 51 patients received ≥240 mg/d for ≤18 months; ages ranged from 16–84 years, with nine patients ≥60 years old. Of these, 27 (ages 17–62 years) were advanced to 320 mg/d, three (ages 20–36 years) then to 400 mg/d, and one (age 36 years) then to 480 mg/d. Most patients improved in primary illness severity (Likert scale, clinician rated). Improvements in negative, depressive, and anxiety symptoms were particularly noteworthy. Treatment was well tolerated; no patients discontinued due to AEs. No clinically significant ECG changes were observed.

Conclusion: Treatment-resistant patients who partially respond to ziprasidone at 160 mg/d may benefit from dosages as high as 480 mg/d, with good toleration.

Funding Source(s): Pfizer

References:


Method: This open-label, naturalistic trial was undertaken because of the prospect of efficacy without concern about venepunctures, organ damage, or weight gain. Generally, it was the first medication trial. Response was assessed retrospectively using an Electronic Medical Record, Behavior2004. Symptom severity was tracked on a Likert scale.

Results: Ages ranged from 5 to 69 years, mean 30, s.d. 14 yrs., 60% were female, over 95% were Caucasian. Dose range was 125 to 5,250 mg/d, mean 1856, s.d. 925. Side effect burden was very low, except for sedation occurring in 9% of patients and used to advantage by dosing at night. Efficacy was good in roughly 50% of patients and partial in an additional 20%. 11% discontinued due to lack of efficacy, 4% due to sedative side effects; 8% were noncompliant.

Conclusion: Levetiracetam was safe, well tolerated and effective in the majority of patients with Bipolar Disorder. It offers an attractive alternative with less side effect burden and greater safety than traditional agents.

Funding Source(s): UCB Pharma

References:

NR375 Tuesday, May 4, 12:00 p.m.–2:00 p.m.
Piribedil: Effects on Cognitive Skill-Learning in Healthy, Elderly Subjects
Sophie Harrois, Psychiatry Department, Chu Reims, 47 Rue Lamouche, Reims 51100, France; Charles S. Peretti, M.D., Fabien Gierski

Educational Objectives:
At the conclusion of this session, the participant would be able to demonstrate that a dopaminergic agonist (Piribedil) can play a positive role in cognitive impairment occurring in healthy old subjects, mainly in problem-solving skill learning.

Summary:
In humans, a decline of dopaminergic transmission with aging is observed and leads us to assume that age-related decline in dopamine activity may contribute to cognitive impairment.

The aim of this study was to examine whether the dopaminergic agonist Piribedil improves cognitive skill learning in healthy elderly subjects.

Subjects were evaluated at baseline, two, and four months according a crossover procedure (placebo or piribedil). A cognitive test battery was used at JO in order to exclude subjects with degenerative disorder. Otherwise, the Tower of Toronto Paradigm was the main test for cognitive skill learning. The number of moves to solution, the optimal solution index (ISO), the optimal and non-optimal solution index (ISONO), the motor time, the cognitive time, and the cognitive time variability were considered.

A significant age x drug interaction on ISO and ISONO was found. The present results suggest that Piribedil showed a beneficial effect on the acquisition of a problem solving, depending on the age, as revealed by solution reliability indexes measures. Piribedil is likely to enhance cognitive skill learning in healthy elderly subjects and give further evidence that age-related dopaminergic decline play an important role in cognitive impairment occurring in normal aging.

References:

NR376 Tuesday, May 4, 12:00 p.m.–2:00 p.m.
Efficacy of Extended-Release Carbamazepine for Pediatric Bipolar Patients
Supported by Shire Pharmaceutical Development, Inc.
Lawrence D. Ginsberg, M.D., Red Oak Psychiatry, 17115 Red Oak Drive, Houston, TX 77090
NR 377 Tuesday, May 4, 12:00 p.m.–2:00 p.m.
Rapid Onset of Absorption With Olanzapine Orally-Disintegrating Tablets
Supported by Eli Lilly and Company
Richard F. Bergstrom, M.D., Lilly Research, Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285; Mark Mitchell, M.S., Jennifer W. Witcher, Ph.D., John P. Houston, M.D., Cindy C. Taylor, Ph.D., Hong Liu-Seifert, Ph.D., Barry Jones, M.D.

Educational Objectives:
At the conclusion of this session, the participant should understand that the clinical perception of a more rapid onset of action of olanzapine ODT than SOT may be due to its more rapid onset of absorption; however, further studies in patient populations are needed.

Summary:
Objective: We examined whether bioavailability data support the clinical perception that olanzapine orally disintegrating tablet (ODT) has a more rapid onset of action than olanzapine standard oral tablet (SOT).
Methods: In three crossover bioequivalence studies, approximately 20 healthy subjects in each study received single-dose olanzapine ODT (5-, 10-, or 20-mg) and the corresponding dose of SOT (1 x 5-mg, 2 x 5-mg, 4 x 5-mg), with >13 days between treatments. Olanzapine plasma concentrations, AUC, and Cmax values were evaluated to assess bioequivalence. Early onset of absorption was assessed using comparative absorption profiles. Results: Olanzapine ODT and SOT were bioequivalent based on AUC and Cmax. Overall, plasma concentration-time profiles and absorption rate constants were nearly identical. For each dose, mean plasma olanzapine concentrations were numerically higher with ODT than SOT during the first hour after administration. For the 5-mg dose, at 15 minutes after administration 79% of subjects had plasma concentrations >0.25 ng/mL with ODT, whereas none did with SOT (p<0.001). These small early concentration differences became indistinguishable before reaching Cmax.
Conclusions: Although olanzapine ODT and SOT are bioequivalent, olanzapine ODT has a more rapid onset of GI absorption than SOT, which is likely attributable to its more rapid disintegration.

References:
References:

NR379 Tuesday, May 4, 12:00 p.m.–2:00 p.m.
Preliminary Pharmacokinetics and Tolerability of Higher Dose Olanzapine
Supported by Eli Lilly and Company
Willie R. Earley, M.D., Health Outcomes, Eli Lilly & Company, Lilly Corporate Center/DC 1748, Indianapolis, IN 46285, Mark Mitchell, M.S., Eva Marquez, M.S., D. Kurtz, M.S., Deborah Falk, M.S., Cindy C. Taylor, Ph.D., Patrizia A. Cavazzoni, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize that although further studies are needed, olanzapine 20–40mg/day had predictable pharmacokinetics and was generally well tolerated.

Summary:
Objective: To investigate the steady-state pharmacokinetics and tolerability of three higher doses of oral olanzapine (20, 30, and 40mg/day) among patients with schizophrenia, schizoaffective disorder, or bipolar mania.
Methods: Thirty-seven stable inpatients were treated with olanzapine 20mg/day for 10 days followed by 10 days of double-blind treatment with olanzapine 20mg (n=12), 30mg (n=11), or 40mg (n=14) daily. For an additional 10 days, 30mg patients received olanzapine 40mg/day (30–40mg); all other patients remained on their same dose. A seven day olanzapine wash-out period followed.
Results: Olanzapine pharmacokinetics appeared linear, with plasma concentrations continuing a dose-proportional increase. Two patients (40mg) discontinued because of an adverse event (akathisia, depressed mood). The most frequently reported adverse events were increased weight (20mg, n=2, 30–40mg, n=3, 40mg, n=2) and sedation (20mg, n=3, 30–40mg, n=2; 40mg, n=2). Five patients (20mg, n=3, 30–40mg, n=2) experienced weight increase >7% from baseline. Four patients (40mg) reported treatment-emergent akathisia (3 of 4 not confirmed by Barnes Akathisia Scale). No clinically important changes were observed in QTc intervals, laboratory parameters, or treatment emergent EPS.
Conclusions: In general, the pharmacokinetic and tolerability profiles of olanzapine 20, 30, or 40mg/day in patients with psychostimulatory disorders were consistent with the known profiles of standard dose olanzapine (5–20mg/day).
Funding Source(s): Supported by funding from Eli Lilly & Company.

References:

NR380 Tuesday, May 4, 12:00 p.m.–2:00 p.m.
Sertraline Versus Venlafaxine Extended Release in Depressed Outpatients
Supported by Pfizer Inc.
Richard C. Shelton, M.D., Department of Psychiatry, Vanderbilt University, 1500 21st Avenue South, #2200, Nashville, TN 37212, Kirsten Haman, Ph.D., Ari Kiev, M.D., Mark H. Rapaport, M.D., Robert M.A. Hirschfeld, M.D., John M. Zajecka, M.D., R. Bruce Lydiard, M.D.

Educational Objectives:
At the conclusion of this session, the participant should better understand the relationship between mechanism of action and response rates with antidepressant drugs.

Summary:
Questions regarding the relationship between mechanism of action and effectiveness of antidepressant drugs still exist. This study was intended to evaluate the relative effect of two antidepressants, sertraline (SER, a serotonin/dopamine uptake inhibitor) and venlafaxine (VEN, a serotonin/norepinephrine uptake inhibitor).
Methods: 160 outpatients with major depression (Hamilton Rating Scale for Depression [HAM-D]>18) were assigned to double-blind treatment with SER (50–150 mg/day) or VEN (75–225 mg/day) for eight weeks. Doses of drug were titrated to the maximum if tolerated. The principal outcome measures included the Quality of Life, Enjoyment, and Satisfaction Scale (Q-LES-Q) and the HAM-D.
Results: 122 (75%) completed eight weeks of treatment with no differences in dropouts between groups (Chi2 p=NS). About 50% of each group achieved the maximum dose. There were no significant differences between groups with regard to overall outcome on any measure (compler or LOCF) or frequency of side effects. Response (>50% reduction in HAM-D) and remission (endpoint HAM-D <8) for the total sample were 52% and 35% (SER) vs. 61% and 47% (VEN) respectively (Chi2 p=NS). Of patients who achieved and maintained the maximum dose of medication for at least 3 weeks, response/remission rates were 64.3% and 52.4% (SER) vs. 73.2% and 53.6% (VEN) (Chi2 p=NS). There were no differences on the Q-LES-Q. However, in the subset of responders and remitters, SER produced significantly greater improvement.
Conclusion: The effectiveness of SER and VEN did not differ significantly. However, dose and duration of treatment had a substantial effect on response and remission rates, especially in the SER group. This should be taken into consideration in future response and remission analyses.
Supported by an independent grant from Pfizer, Inc.

References:

NR381 Tuesday, May 4, 12:00 p.m.–2:00 p.m.
Clinical Status and Tolerability After the First 12 Months of Treatment
Supported by Eli Lilly and Company
Padraig Wright, M.D., Lilly Research, Eli Lilly and Company, Erl Wood Manor, Sunning Hill Road, Windlesham GU208PH, United Kingdom; Diego Novick, M.D., Mark Belger, Ph.D., Mark Ratcliffe, M.D.
Educational Objectives:

At the conclusion of this session, the participant should understand how 12 months of antipsychotic treatment in actual European outpatient settings affect the clinical effectiveness, tolerability and treatment continuation of people with schizophrenia.

Summary:

**Objective:** To describe clinical status and tolerability changes over twelve months of antipsychotic treatment, for schizophrenic patients remaining on their initial treatment.

**Methods:** Pan-European SOHO1 is a 3-year, perspective, outpatient, observational study. Patients' clinical status was defined as improved if CGI-S (Clinical Global Impression Schizophrenia scales) 2 score reduced by 2 points, when patients were markedly ill to among the most severely ill, or by 1 point, when patients were borderline ill to moderately ill, at baseline.

**Results:** 8,530 monotherapy patients were followed for twelve months, 63% of which remained on their baseline antipsychotic. This varied across treatments; olanzapine (65%), clozapine (71%), amisulpride (50%), depot typicals (57%), oral typicals (54%), quetiapine (42%) and risperidone (61%).

Overall CGI-S symptom improvements ranged from 50% of patients (depot typicals) to 70% (olanzapine). Similar results were observed in positive, negative, cognitive and depressive CGI-S symptoms. Extrapyramidal symptoms also varied (range: olanzapine (8% of patients) to depot typicals (35%)). All patients experienced weight gain (range: olanzapine (3.16kg) to quetiapine (0.62kg)).

**Conclusion:** Approximately 2/3 of patients remain on their baseline antipsychotic, having reasonable clinical effectiveness and tolerability, after twelve months of treatment. Olanzapine appears having a range of modest effectiveness and tolerability advantages over other first line antipsychotics.

**Funding Source(s):** Supported by funding from Eli Lilly & Company

**References:**


in comparison to newer anticonvulsants, while newer anticonvulsants were perceived to be safer and more tolerable than older anticonvulsants (Cochran-Mantel-Haenszel, P=.001). Efficacy was ranked as the most important factor in the choice of an anticonvulant in treating bipolar patients.

Conclusions: The results from this survey indicate that a majority of respondents have used a combination of anticonvulsants in the treatment of bipolar disorder. Newer anticonvulsants were considered to be safer and more tolerable than older anticonvulsants. However, efficacy, which was determined to be the most important factor in psychiatrists’ choice of anticonvulant, was rated more favorably for older anticonvulsants.

Funding Source(s): Shire

References:

NR385 Tuesday, May 4, 12:00 p.m.–2:00 p.m.
Flexible-Dose Aripiprazole in Psychosis of Alzheimer’s Dementia
Supported by Bristol-Meyers Squibb and Otsuka Pharmaceutical Co., Ltd.
Joel E. Streim, M.D., Department of Psychiatry, University of Pennsylvania, 3600 Market Street, Room 3055, Philadelphia, PA 19104; Christopher Breder, M.D., Rene Swanink, M.S.C., Robert D. McQuade, Ph.D., Taro Iwamoto, Ph.D., William H. Carson, Jr., M.D., Elyse G. Stock, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to better understand the efficacy, safety, and tolerability of aripiprazole in patients with psychosis associated with Alzheimer’s dementia.

Summary:
Objective: To evaluate flexible-dose aripiprazole for treatment of institutionalized patients with psychosis of AD.
Methods: 256 institutionalized patients with psychosis of AD were randomized to placebo or flexible dose of aripiprazole (starting dose, 2mg/d) for 10 weeks. Efficacy assessments included the NPI-NH, BPRS, CGI, CMAI, and Cornell Scale for Depression in Dementia.
Results: The mean aripiprazole dose used at study end was 8.6 mg/day (range, 2–15 mg/day). Comparable improvements in NPI-NH Psychosis subscores were observed at week 10 in aripiprazole and placebo groups. Aripiprazole-treated patients showed significant improvement compared with placebo in NPI-NH (−16.4 vs −10.0, p<.0009) and BPRS (−7.7 vs −5.1, p<.031) total scores. Significant improvements in agitation and mood symptoms were observed using CMAI and Cornell Depression scales and CGI-I scores. Discontinuation rates due to AEs were similar in the two groups (aripiprazole, 13%; placebo, 8%), EPS-related adverse events were comparable in the two treatment groups (5% with aripiprazole and 4% with placebo).
Conclusion: Aripiprazole treatment resulted in significant improvement over placebo in NPI-NH and BPRS total scores in institutionalized patients with psychosis of AD. The improvement was most pronounced for agitation, behavioral and mood symptoms. Aripiprazole treatment was well tolerated in this elderly population.
Funding Source(s): Bristol-Myers Squibb Company and Otsuka Pharmaceutical Co., Ltd.

References:
Objective: The initial goal of antidepressant therapy is full remission. Recent work suggests that there may be modest, albeit significant differences between various types of antidepressants. A meta-analysis using individual patient data from 12 double-blind, randomized, controlled trials of mirtazapine versus SSRIs was conducted in more than 2,500 depressed patients to compare remission as a measure of efficacy.

Methods: Remission rates (HAMD-17 ≤ 7 or MADRS ≤ 12) were compared at weeks 1-6 and time to sustained remission were graphically displayed using the Kaplan-Meier method. Predictive values of early response for later remission at week 6 also were calculated.

Results: Remission rates after 6 weeks of therapy were 38.8% and 34.7% in the mirtazapine- and SSRIs-treated groups respectively. The difference between the two groups was statistically significant in favor of mirtazapine at all assessments and across time (p < 0.03; Logrank test). This advantage was largely explained by the onset of remission during the first three weeks of treatment (p < 0.001).

Conclusion: Therapy with mirtazapine resulted in a significantly greater overall probability of remission and a significantly more rapid onset of clinical improvement when compared to therapy with the SSRIs.

References:

Objective: To review baseline levels of total cholesterol (TC) and triglycerides in patients with schizophrenia who participated in ziprasidone clinical trials and changes in these parameters associated with ziprasidone.

Methods: This was a secondary analysis of measurements (random times at study visits) of baseline TC and triglyceride levels and of changes from baseline to last observation from short-term (4–6 weeks), fixed-dose, placebo-controlled (STFDPC) trials and long-term (6 month) trials.

Results: In STFDPC trials, median baseline TC and triglyceride levels in patients receiving ziprasidone (n=682) were 185 mg/dL and 126 mg/dL; median changes in TC and triglycerides were −3 mg/dL and −6 mg/dL. In long-term trials (n=1009), median TC change was −10 mg/dL from a baseline of 196 mg/dL; median change in triglycerides was −7 mg/dL from a baseline of 132 mg/dL. Mean lipid changes in long-term trials were similar with or without adjustment for weight change.

Conclusion: Baseline median TC and triglyceride levels in ziprasidone trials suggest a high prevalence of lipid levels in excess of National Cholesterol Education Program thresholds in this population. Ziprasidone was not associated with increases in lipids in short- or long-term trials. Reductions in TC and triglycerides in long-term trials were independent of weight change.

Funding Source(s): Pfizer, Inc.

References:
subjects treated with mirtazapine than subjects treated with SSRI during the first three weeks of treatment (p ≤ 0.001).

The highly consistent findings in these survival analyses showed a clear advantage of mirtazapine over the SSRI, indicating a faster onset of action for mirtazapine compared with the SSRI.

The results of the meta-analysis regarding early response to treatment were considered meaningful based on the absence of any notable signs of heterogeneity.

References:

NR389 Tuesday, May 4, 12:00 p.m.–2:00 p.m.
Differences in Sexual Dysfunction Between Men and Women With Depression
Sidney H. Kennedy, M.D., Department of Psychiatry, University of Toronto, 399 Bathurst Street, Toronto, ON M5T 2S8, Canada; Kari Fulton, B.A., Shahyary Rafai-Tari, M.S.C., Andrea Greene, B.A., Nicole Cohen, B.A., Michael R. Bagby, Ph.D.

Summary:
Objective: The primary purpose of the study was to compare the effects of sexual dysfunction on bupropion and paroxetine in depressed men and women before and over the course of an 8-week trial. A secondary purpose was to compare the Sex Effects (Sex FX) to the Investigator Sexual Desire Functioning assessment (IRSD/F) to establish concurrent validity of sensitivity to change.

Method: Multicentre, double-blind, 141 patients with DSM-IV major depression, randomly assigned to a flexible dosing of bupropion SR (150–300mg) or paroxetine (20–40mg). Patients were assessed at baseline and after 2, 4, 6 and 8 weeks using the 17-item Hamilton Rating Scale for Depression (HRS), the Sex Effects scale of sexual dysfunction in males and females (Sex FX M/F), and the IRSD/F.

Results: Bupropion and paroxetine were equally effective in the treatment of depressive symptoms. Women had significantly higher levels of sexual dysfunction (SD) than men at baseline. Bupropion SR did not significantly alter SD scores in men and women. In contrast, there was an increase in SD over time in men but not in women treated with paroxetine. For both men and women, the Sex FX was positively correlated with the IRSD/F.

Conclusion: Rates of SD differed between men and women before and during antidepressant treatment. While women did not report any change in sexual dysfunction, antidepressant induce or exacerbated sexual dysfunction was only apparent in males treated with paroxetine. Bupropion did not significantly alter SD in men or women. Results for Sex FX correlating highly with IRSD/F indicate its a sensitive and valid measure of change in SD.

References:

NR390 Tuesday, May 4, 12:00 p.m.–2:00 p.m.
Injectable Ziprasidone in the Psychiatric Emergency Room: Expanded Sample
Supported by Pfizer Inc.
Horacio Preval, M.D., Psychiatry Department, SUNY, Stony Brook, HSC-T10, Stony Brook, NY 11794; Steven G. Klotz, M.D., Robert Southard, N.P., Andrew J. Francis, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to discuss the utility of IM ziprasidone versus conventional sedatives for patients with severe agitation including that from alcohol or substance intoxication.

Summary:
Objective: Injectable atypical neuroleptics may supplant benzodiazepine and/or butyrophenone alternatives. Published studies of intramuscular [IM] ziprasidone excluded severe psychiatric agitation [AGIT], and that from alcohol [ETOH] or other substances [SUBS].

Method: We report additional data on BARS agitation scores [min=1, max=7] and duration of physical restraints in a naturalistic Psychiatric ER study. Dosages were 20mg for ziprasidone, and 40mg for conventional IM sedatives [76% haloperidol and/or lorazepam].

Results: Baseline BARS scores were high for AGIT [N=72], ETOH [N=10] and SUBS [N=28] [respective means: 6.5, 6.9, 6.6, P=NS]. Ziprasidone decreased agitation rapidly [respective means: 5.6, 5.3, 5.8 at 15min (P<.05), and 4.2, 4.1, 4.1 at 30min (P<.01)]. At 2 hr, scores were 2.6, 2.1, and 2.3 (P<.01). For conventional sedatives [N=9] baseline scores were 6.6, then 5.7 at 15min, 4.2 at 30min, and 2.9 at 2hr [P<.02 vs ziprasidone]. Restraint duration decreased from 91±6 to 53±3 min with ziprasidone (P<0.01) and varied with conventional sedatives (54±14 min, P=NS). Of 19 EKGs, none had prolonged QTc; one dystonic reaction occurred with ziprasidone.

Conclusion: IM ziprasidone appears effective for severe agitation including that from alcohol or substance-induced intoxication. It may lead to reduced time in restraints compared with conventional agents.

Funding Source(s): Pfizer

References:

NR391 Tuesday, May 4, 12:00 p.m.–2:00 p.m.
Course of Weight and Metabolic Benefits One Year After Switching to Ziprasidone
Supported by Pfizer Inc.
Peter J. Weiden, M.D., Department of Psychiatry, SUNY Health Science Center at Brooklyn, 450 Clarkson Avenue, Box 1203, Brooklyn, NY 11203; David G. Daniel, M.D., Antony D. Loebel, M.D., Lewis Warrington, Ph.D., Judith Dunn, Ph.D., Stephen R. Murray, M.D.

Educational Objectives:
At the conclusion of this session, the participant should understand the long-term impact of side effects, including weight and metabolic parameters, after the switch to ziprasidone.
Summary:

Objective: To determine the long-term course of short-term improvements in weight and metabolic side effects among outpatients recently switched to ziprasidone.

Methods: Three open-label, flexible-dose continuation studies enrolled stable completers of 6-week trials of outpatients who were switched from either conventional (n=71), olanzapine (n=71), or risperidone (n=43) to ziprasidone. Follow-up to one year of ziprasidone monotherapy (median 30.5 weeks) permitted longitudinal assessment of improvement in weight and metabolic side-effect profile using ITT analysis.

Results: The main finding was continued weight loss and lowering of BMI over one-year for patients who were switched from risperidone or olanzapine. For the pre-switch olanzapine group, additional weight loss was 5.7 lb (P<0.0001) over and above the initial 6-week weight loss of 3.7 lb. For the pre-switch risperidone group, the additional weight loss was 9.3 lb (P<0.001) over and above the initial 2.0-lb weight loss. The metabolic improvements in triglycerides and cholesterol obtained from the six-week switch were sustained over one year. For example, the reduction in median triglycerides was 31.0 mg/dL (P=0.0001) for the pre-switch olanzapine group, and was 17.0 mg/dL (P=0.05) for the pre-switch risperidone group.

Conclusions: Patients switched from olanzapine or risperidone to ziprasidone continued losing weight for up to 1 year. Other initial 6-week improvements in metabolic parameters were sustained during long-term ziprasidone. References: Pfizer Inc

References:

NR392 Tuesday, May 4, 12:00 p.m.—2:00 p.m.
Sleep Improvements During Treatment of Depression With Mirtazapine or SSRIs
Andrew Winokur, M.D., Psychiatry Department, University of Connecticut, 10 Talcott Notch Road, MC-6415, Farmington, CT 06030-6415; Albert J. Schutte, M.D., Argen P.P. van Willigenburg

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the differential effects of mirtazapine and SSRIs on patients’ sleep during short-term treatment of depression, and subsequently to make informed therapy choices for individual depressed patients presenting with pronounced sleep-related complaints.

Summary:

Aim: To compare the effects of mirtazapine and SSRIs on sleep during short-term treatment of depression.

Method: A pooled analysis was performed using individual patient data from 11 eligible RCTs comparing mirtazapine (n=1,263) and one of the SSRIs (fluoxetine, paroxetine, sertraline and fluvoxamine; n=1,269), in major depression. Improvements in sleep at Weeks 1, 2, 4, and 6 assessments (ITT group, LOCF approach) were assessed by changes from baseline in HAMD sleep disturbance factor using fitting ANCOVA model and percentages of patients with ≥50% improvement in sleep disturbance factor using the Cochran-Mantel-Haenszel test.

Results: At all assessment points, changes from baseline were significantly larger for the mirtazapine-compared with the SSRIs-treated group (estimated treatment difference range: -0.72 (Week 1) to -0.46 (Week 6); 95% CI range: -0.84 to -0.60 (Week 1) to -0.60 to -0.33 (Week 6)). Mirtazapine treatment was also associated at all assessments with a significantly higher percentages of patients attaining ≥50% improvement from baseline in sleep disturbance factor score (all P≤0.01).

Conclusions: Mirtazapine was associated with significantly larger and faster attained improvements in sleep disturbances compared with SSRIs during short-term treatment of depression, confirming their differential effects on sleep. The results could be related to mirtazapine-induced improvements in objective sleep parameters in depressed patients.

References:

NR393 Tuesday, May 4, 12:00 p.m.—2:00 p.m.
Dov 216303, a Triple Reuptake Inhibitor: First in Human Studies

Supported by Dov Pharmaceutical, Inc
Arnold Lifpa, Ph.D., Dov Pharmaceutical, Incorporated, 433 Hackensack Avenue, Hackensack, NJ 07601; Bernard Beer, Jill Stark, Philip Krieter, Ph.D., Pal Czobor, Ph.D., Phil Skolnick, Ph.D.

Educational Objectives:

At the conclusion of this session, participants will understand the safety, tolerability, pharmacokinetic profile, and rationale for developing DOV 216,303. This potential antidepressant inhibits the reuptake of the three biogenic amines (norepinephrine, serotonin, and dopamine) most closely linked to depression.

Summary:

Objective: To examine the safety, tolerability and pharmacokinetic profile of DOV 216,303, a “triple” reuptake inhibitor.

Method: The study was conducted at the Parexel CEMAF Clinical Facility, Poitiers, France, Subjects were healthy male volunteers, 18–35 years old. Both the single and multiple dose studies were randomized, double-blind, placebo-controlled trials. The single dose study consisted of 5, 10, 25, 50, 100, and 150 mg of DOV 216,303, or placebo. In the multiple dose study, volunteers received total daily doses of 50, 75, and 100 mg of drug or placebo for 10 days.

Results: No drug-related effects on vital signs, EEG, ECG, hematological or clinical chemistry measures were reported. Plasma levels of DOV 216,303 were dose proportional following both single and multiple dosing. DOV 216,303 was well tolerated in both the single and multiple dose studies, with a low incidence of adverse events.

Conclusions: At doses ≥10 mg, plasma levels of DOV 216,303 are sufficient to inhibit the norepinephrine, serotonin and dopamine transporters. The safety and tolerability of DOV 216,303 indicates this molecule may be used to examine the hypothesis that a “triple” reuptake inhibitor may be a more effective antidepressant than either single or dual reuptake inhibitor.

Funding Source(s): Dov Pharmaceutical, Inc.
References:


NR394 Tuesday, May 4, 12:00 p.m.—2:00 p.m.
Pharmacotherapy for Bipolar Disorder and Comorbid Conditions: STEP-BD Data
Naomi M. Simon, M.D., Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WANG ACC 815, Boston, MA 02114; Gary S. Sachs, M.D., Joseph R. Calabrese, M.D., Andrew A. Nierenberg, M.D., Michael W. Otto, Ph.D., Roger D. Weiss, M.D., Michael S. Bauer, M.D., Sachiko Miyahara, M.S., Stephen R. Wisniewski, Ph.D., Mark H. Pollack, M.D., Michael E. Thase, M.D., Jane Kogan, Ph.D., Ellen Frank, Ph.D.

Educational Objectives:

1. At the conclusion of this session, the participant should understand the impact of comorbid disorders on pharmacotherapy selection for patients with bipolar disorder.

2. By the end of this session, the participant should understand the treatment options for patients with bipolar disorder.

3. The participant should be able to apply the findings to their practice setting.

4. The participant should be able to discuss the role of pharmacotherapy in the treatment of bipolar disorder.

5. The participant should be able to discuss the role of comorbid disorders in the treatment of bipolar disorder.

6. The participant should be able to discuss the role of pharmacotherapy in the treatment of comorbid disorders.

7. The participant should be able to discuss the role of pharmacotherapy in the treatment of bipolar disorder and comorbid disorders.

8. The participant should be able to discuss the role of pharmacotherapy in the treatment of bipolar disorder with comorbid disorders.

9. The participant should be able to discuss the role of pharmacotherapy in the treatment of bipolar disorder and comorbid disorders.

NR395 Tuesday, May 4, 12:00 p.m.—2:00 p.m.
Pilot-Controlled Trial of Lamotrigine Adjuvant Treatment in Schizophrenia
Supported by GlaxoSmithKline
Agnes Vass, M.D., Psychiatry Department, Herzog Memorial Hospital, PO Box 35300, Jerusalem 91351, Israel; Ilana Kremer, M.D., Ilena Gurelik, M.D., Monica Blenuar, M.D., Gali Bar, B.A., Daniel Javitt, M.D., Uriel Heresco-Levy, M.D.

References:


NR396 Tuesday, May 4, 12:00 p.m.—2:00 p.m.
Double-Blind Dose-Finding Study of Docosahexaenoic Acid in Major Depression
David Mischoulon, M.D., Department of Psychiatry, Massachusetts General Hospital, Wac 812, 15 Parkman Street, Boston, MA 02114; Jessica L. Murakami, B.A., Yasmin Mahal, B.A.; Catherine Best, M.S., Michael Lapajone, M.D., Andrew A. Nierenberg, M.D., Maurizio Fava, M.D., Jonathan E. Alpert, M.D.
Educational Objectives:

At the conclusion of this session, the participant should understand the evidence in support of omega-3 fatty acids as a potential treatment for depression.

Summary:

Background: Recent evidence suggests effectiveness of omega-3 fatty acids for bipolar disorder, unipolar depression, and psychotic disorders, sometimes with doses as low as 1–2g/day. We undertook a pilot dose-finding study of docosahexaenoic acid (DHA) to determine its dose/response relationship in the treatment of major depressive disorder (MDD).

Methods: We recruited 34 adults, ages 18–80 (47% women; mean age 42±14 years), diagnosed with MDD by the Structured Clinical Interview for DSM-III-R, with a 17-item Hamilton-Depression Rating Scale (HAM-D-17) score ≥18 at entry. Subjects were randomized into three arms. The dosing was double blind. One group (n=14) received 1g/day of DHA for 12 weeks; the second group (n=10) received 2g/day of DHA; and a third group (n=10) received 4g/day of DHA. Subjects were administered a questionnaire about dietary habits, in particular about consumption of omega-3-rich foods, so as to control for any dietary influence on the response to the study medication. Outcome was measured by improvement in HAM-D-17, Beck Depression Inventory (BDI), and Clinical Global Impressions (CGI). Response was defined as ≥50% decrease in HAM-D score.

Results: Among study completers, the group receiving 1g/day showed an 83% response rate; the group receiving 2g/day showed a 40% response rate; and the group receiving 4g/day showed a 0% response rate. Intent-to-treat (ITT) analysis showed a similar trend (45% response rate for 1g/day, 33% for 2g/day, and 14% for 4g/day). Among completers, the low and intermediate dose groups had a statistically significant improvement in HAM-D-17 scores (p<0.05); in the ITT sample, improvement in HAM-D-17 scores reached significance for all 3 groups (p<0.05). Although side effects were more common at higher DHA doses, there was no significant difference in dropouts due to side effects in the intermediate and higher dose groups.

Conclusions: DHA may work best at lower doses. At higher doses, we may be observing an "overcorrection effect" with regard to fatty acid imbalance. Further comparison between the different types of omega-3 fatty acids and placebo is needed, as well as investigation of the psychotropic mechanisms of action of the omega-3s.

Funding Source(s): NARSAD

References:


NR398
Tuesday, May 4, 12:00 p.m.–2:00 p.m.
Low Manic Switch-Rate During SSRI Treatment of Bipolar Major Depression
Supported by Eli Lilly and Company

Justine Shults, Ph.D., University of Pennsylvania, 610 Blockley Hall, 423 Guardian Drive, Philadelphia, PA 19104; Jay D. Amsterdam, M.D.

Educational Objectives:

At the conclusion of this session, the participants should have a more comprehensive understanding of the nature and frequency of manic switch episodes during SSRI treatment of BP II MDE. They will also learn about SSRI monotherapy of BP II MDE, and how to assess patients for the presence of SSRI-induced mood induction.

Summary:

Psychotic major depression (PMD) has been characterized by elevated glucocorticoid activity and neuropsychological impairment. We have reported in small pilot studies that the glucocorticoid antagonist, mifepristone, may be rapidly effective in ameliorating the psychotic symptoms in the disorder. We now report on a double-blind comparison of eight days of 600 mg/day of mifepristone vs placebo added on to stable, but ineffective medication in 30 patients. Patients were assessed both before and after treatment for cortisol rhythm from 1800hr to 0900hr, neuropsychological testing, and functional magnetic resonance imaging. Baseline data were also collected on 30 nonpsychotic patients and 30 healthy controls. At baseline, PMD patients demonstrated elevated cortisol activity and impairment on frontal and hippocampal mediated tasks compared to the other two groups which did not differ between them. Mifepristone resulted in a significantly greater likelihood of demonstrating a 30% improvement in BPRS total score (p<.001) and a 50% improvement on the BPRS positive symptom scale (p<.001). In addition, as compared with placebo and with baseline, there was a normalization of the cortisol rhythm curve from 0100hr to 0900hr in the patients treated with the active drug. These data suggest the drug may be rapidly effective in this difficult to treat disorder.

Funding Source(s): NIH-MH 50604

References:


NR397
Tuesday, May 4, 12:00 p.m.—2:00 p.m.
Mifepristone in Psychotic Major Depression

Alan F. Schatzberg, M.D., Department of Psychiatry, Stanford University, 401 Quarry Road, Stanford, CA 94305-5717; Ben Flores, M.D., Hugh B. Solvason, M.D., Jennifer Keller, Ph.D., Heather K. Gumina, M.A.

Educational Objectives:

At the conclusion of this session, the participant should be able: (1) to review the potential role of excessive HPA axis in psychotic major depression; (2) to assess potential efficacy of glucocorticoid antagonists in PMD

Summary:

Psychiatric major depression (PMD) has been characterized by elevated glucocorticoid activity and neuropsychological impairment. We have reported in small pilot studies that the glucocorticoid antagonist, mifepristone, may be rapidly effective in ameliorating the psychotic symptoms in the disorder. We now report on a double-blind comparison of eight days of 600 mg/day of mifepristone vs placebo added on to stable, but ineffective medication in 30 patients. Patients were assessed both before and after treatment for cortisol rhythm from 1800hr to 0900hr, neuropsychological testing, and functional magnetic resonance imaging. Baseline data were also collected on 30 nonpsychotic patients and 30 healthy controls. At baseline, PMD patients demonstrated elevated cortisol activity and impairment on frontal and hippocampal mediated tasks compared to the other two groups which did not differ between them. Mifepristone resulted in a significantly greater likelihood of demonstrating a 30% improvement on BPRS total score (p<.001) and a 50% improvement on the BPRS positive symptom scale (p<.001). In addition, as compared with placebo and with baseline, there was a normalization of the cortisol rhythm curve from 0100hr to 0900hr in the patients treated with the active drug. These data suggest the drug may be rapidly effective in this difficult to treat disorder.

Funding Source(s): NIH-MH 50604

References:


fluoxetine did not differ from that seen at baseline visits. Only five patients (13.5%) had a YMR＞12 at any visit. GEE analysis showed no change in mean YMR compared with baseline (p=0.93). There were no manic episodes, and only three patients (7.3%) met DSM-IV criteria for hypomania.

Conclusion: These data suggest a low manic switch rate during SSRI monotherapy of BP II MDE.

Funding Source(s): Grants from Eli Lilly & Company and NIMH R01 MH 060353

References:

**NR399**
Tuesday, May 4, 12:00 p.m.–2:00 p.m.
Risperidone and 9-OH Risperidone Have no Thrombogenic Propensity In-Vitro Supported by Johnson & Johnson
Fred de Clerck, Ph.D., Johnson and Johnson, Turnhoutseweg 30, Beersel b-2340, Belgium, Yves Somers, Marielle Eerdekens, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize the absence of direct thrombogenic effects of risperidone and 9-OH risperidone on human platelet function, plasma coagulation, and fibrinolysis at in vitro concentrations markedly exceeding therapeutic plasma levels in psychiatric patients.

Summary:
Objective: To validate the potential association of antipsychotic drugs with thrombotic events in patients, we evaluated the in vitro effects of risperidone and 9-OH risperidone in comparison with reference drugs on parameters relevant for thrombogenesis in man.

Results: At concentrations largely exceeding therapeutic free drug plasma levels (~4000ng/ml), neither risperidone nor 9-OH risperidone induces human platelet shape change or aggregation, amplifies reactions to low concentrations of ADP or modifies responses (adhesion, aggregation, TXB2 production) to fully active doses of collagen or ADP. Cyclo-oxygenase, TXA2-synthase, 12-lipoxygenase in human platelets and prostacyclin synthase in rat aortic rings are not affected either. Additionally, the compounds do not modify human plasma coagulation via the intrinsic or extrinsic pathways (APTT, TT, PTT) or affect fibrinolysis in human diluted whole blood with and without acceleration by rt-PA. As expected from their potent antagonism at 5-HT2A receptors, low concentrations of both drugs attenuate the modest human platelet aggregation reaction to 5-HT.

Conclusion: This study shows that risperidone and 9-OH risperidone—at in vitro concentrations largely in excess of therapeutic plasma levels in man—do not affect relevant processes modulating clinical thrombotic events.

Funding Source(s): Johnson & Johnson Pharmaceutical Research and Development

References:

**NR400**
Tuesday, May 4, 12:00 p.m.–2:00 p.m.
Effects of Risperidone on Cognition in Children With Disruptive Behaviors Supported by Janssen Pharmaceutica and Research Foundation
Gahan J. Pandina, Ph.D., Medical Affairs Department, Janssen Pharmaceutica, Inc., 1125 Trenton- Harbourton Road, Titusville, NJ 08560; Robert Bildner, Ph.D., Philip D. Harvey, Ph.D., Richard S.E. Keefe, Ph.D., Michael G. Aman, Ph.D., Georges Gharabawi, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize the effects of risperidone on cognitive function in pediatric patients with disruptive behavior disorders, particularly regarding the risk-benefit ratio of risperidone-associated somnolence and cognitive function.

Summary:
Objective: To assess the effects of risperidone on cognition in children with disruptive behavior disorders (DBD) and subaverage intelligence.

Methods: Data were from two double-blind, placebo-controlled, short-term studies, their one-year, open-label extensions, and a third one-year open-label study. Cognitive measures included verbal learning test for children (VL/T-C) and continuous performance test (CPT) for attention. Assessments were performed at baseline, six weeks (double-blind endpoint), and one year (open-label endpoint).

Results: Short-term Double-Blind Studies: Subjects (mean age, 8.5 years, 79% males, IQ = 67 ± 13) received risperidone (n=108) or placebo (n=120). No significant decrement was noted in CPT scores in either group; several measures improved (P<0.05). Short-term verbal memory improved significantly in both groups (P<0.0001). Long-term verbal memory improved significantly with placebo (P<0.001) and risperidone, but not significantly (P=0.18). Somnolence was reported by 46% of risperidone- and 12% of placebo-treated patients. Long-term Open-Label Studies: Subjects (n=688; mean age 9.4 years; 82% males; IQ=65±13) received risperidone. There was no significant attention decrement (CPT) most measures increased (P<0.05). Short- and long-term verbal memory also improved (P<0.0001). Somnolence was reported by 33% of patients.

Conclusions: These data suggest that attention and verbal learning in children with DBD are preserved during risperidone treatment, despite an increase in somnolence.

Funding Source(s): Supported by Janssen Pharmaceutica Products, L.F.

References:

**NR401**
Tuesday, May 4, 12:00 p.m.–2:00 p.m.
Risperidone Versus Haloperidol in Acute Psychotic Inpatients: Effect on Dimensional Psychopathology Factors
Giuseppe Bersani, Psychiatry Department, Lasapienza University, Via di Torre Argentina 21, Rome, IT 00100, Italy; Francesca Paolitti
NR402  Tuesday, May 4, 12:00 p.m.–2:00 p.m.
Use of Zonisamide in Depressed and Bipolar Adults: A Chart Review Study
Supported by Elan Biopharmaceuticals

Arnold W. Mech, M.D., Mech Psychiatric Associates, 4100 W L5TH St #220, Plano, TX 75093

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the potential utility of zonisamide in treating patients with bipolar disorder and major depressive disorder.

Summary:
Objective: To evaluate safety and efficacy of in depressed and bipolar adults.
Method: This chart review included patients from an outpatient private practice ≤17 years of age with bipolar disorder or major depressive disorder treated with zonisamide as adjunctive therapy between May 2003 and August 2003. Charts were reviewed for adverse events (AEs) and response to zonisamide therapy based on Beck Depression Inventory (BDI), Young Mania Rating Scale (YMRS), and Barkley Inventory scores at baseline and after six weeks of therapy.
Results: The charts of 40 patients (29 women, 11 men) were reviewed. Thirty-two patients had a diagnosis of major depression; eight had a diagnosis of bipolar disorder. The most common AE was weight change. Seventeen patients lost weight with a mean weight loss of 8.2 pounds, 11 gained weight with a mean weight gain of 7.9 pounds, and 12 experienced no weight change. All patients were receiving at least one concomitant medication that is typically associated with weight gain. Other common AEs included increased anxiety (n=5), nausea (n=3), and insomnia (n=2). Improvements in mean BDI (baseline: 24, 6-week: 18), YMRS (baseline: 12, 6-week: 10), and Barkley Inventory (baseline: 19, 6-week: 14) scores were reported with zonisamide therapy.

Conclusions: These results suggest that zonisamide is safe in treating patients with bipolar disorder and major depression. For patients whom weight gain is a concern, addition of zonisamide may limit weight gain associated with other therapeutic agents.

References:

NR403  Tuesday, May 4, 12:00 p.m.–2:00 p.m.
Tiagabine Augmentation for Treatment-Refractory Anxiety Disorders
John J. Worthington III, M.D., Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC 815, Boston, MA 02114; Gustavo D. Kinrys, M.D., Naomi M. Simon, M.D., Hannah Reese, B.A., Maria Melo, B.A., Diana Fischmann, B.A., Mark H. Pollack, M.D.

Educational Objectives:
To recognize the potential use of tiagabine in refractory anxiety disorder patients; to appreciate the high rate of partial response to initial treatment of anxiety disorders.

Summary:
Objective: Despite the available treatments for the anxiety disorders, many patients remain symptomatic after initial intervention. Thus, there remains a need to develop additional strategies to improve outcome for treated anxiety disorder patients. Tiagabine is a selective GABA reuptake inhibitor. We examined the effect of Tiagabine augmentation of anxiolytic pharmacotherapy in patients with anxiety disorders remaining symptomatic despite initial therapy.

Method: Retrospective chart review of augmentation with Tiagabine in adult outpatients with anxiety disorders (N=19), who were not full responders to a variety of anxiolytic medications. Given the range of anxiety disorders represented, the primary outcome measures for this study were the Clinical Global Impression of Improvement Scale (CGI-I) and Clinical Global Impression of Severity Scale (CGI-S).

Subjects: Mean age of the subjects was 36 ± 11 years, 68% were male.

Results: The mean dose of Tiagabine was 17 ± 7 mg per day, with a range of 8 to 32 mg per day and the mean duration of treatment assessed was 24 ± 11 weeks. Seven of 19 subjects (37%) were much or very much improved (CGI-I 1 or 2) in terms of their anxiety symptoms. The mean CGI-I was 2.6 ± 1.1 and the mean CGI-S at baseline was 5.7 ± 0.7, which fell to 3.8 ± 1.6 at endpoint (t = 4.7, df = 18, p < .001). Five of the 13 patients complained of sedation on Tiagabine, but none of them discontinued the medication because of it.

Conclusion: Results from this open, retrospective case series, suggest that Tiagabine may effectively augment response to anxi-
References:

NR404  Tuesday, May 4, 12:00 p.m.—2:00 p.m.
Levetiracetam as an Add-On in Adults and Children With Bipolar Disorder
Supported by UCB Pharma
Ali Ahmadi, M.D., Macon Psychiatry Center PC, 754 First Street, Suite 101, Macon, GA 31201; Sima Ekhtiar, M.S.

Educational Objectives:
At the conclusion of this session, the participant should recognize levetiracetam as a potentially valuable add-on treatment for the care of bipolar disorder patients.

Summary:
Objective: Systematic examination of levetiracetam's (LEV) effect in adults and children with bipolar disorder.

Introduction: LEV is a mechanistically unique antiepileptic drug. LEV's utility as a mood stabilizer in bipolar disorder (BDP) has been reported previously.

Methods: Systematic chart review of 30 patients (19 adult, 11 children) was performed to capture history, demographics, response to other medications, target symptoms for LEV use, LEV dosage, and response to LEV. Response was rated from 0 (no response) to 4 (excellent response), per physician evaluation and patient reporting.

Results: Mean response to LEV overall was 2.9 (range 1–4). BDP II and BPD NOS patients benefited slightly more than BPD I (3.05, 2.9, and 2.6 respectively). When evaluated by age, patients aged 16 and older showed more improvement than younger patients did; however, the difference was small (3.03 vs. 2.68). Targeted symptoms most commonly reported as improved included mood instability, irritability, impulsivity, poor sleep, and racing thoughts. No adverse events were reported. Average daily dose was 1355 mg/day (range 250–3000mg) in adults (ages 16–50) and 430 mg/day (range 250–750mg) in children (ages 5–15).

Conclusion: LEV improved targeted symptoms of BPD when added to existing therapy. LEV was extremely well tolerated in both age groups.

Funding Source(s): Funding support provided by UCB Pharma

References:

NR406  Tuesday, May 4, 12:00 p.m.—2:00 p.m.
Effective Dose of Quetiapine in the Treatment of Bipolar Mania
Supported by AstraZeneca Pharmaceuticals
Joseph F. Goldberg, M.D., Department of Psychiatry, Zucker Hillside Hospital, 79-59 263rd Street, Glen Oaks, NY 11004

Educational Objectives:
At the conclusion of this session, the participant should: (1) have a clear understanding of quetiapine dosing for the treatment of mania in bipolar disorder; and (2) be able to select doses of quetiapine for the treatment of bipolar disorder that are effective and well tolerated.

Summary:
Objective: Establish the effective dose of quetiapine for the treatment of mania.

Methods: Patients with bipolar I mania were flexibly dosed with quetiapine as monotherapy (for 12 weeks) or in combination with lithium (0.7–1.0 mEq/L) or divalproex (50–100 μg/mL) (for three or six weeks) in double-blind studies. Quetiapine target dose was increased in steps of 100 mg/day at Day 4, up to 600 mg/day at Day 5, and up to 800 mg/day thereafter.

References:
Results: Administration of quetiapine achieved a statistically significant improvement in change from baseline in YMRS score within the first week and onward, as monotherapy or in combination with lithium or divalproex. The average quetiapine dose in responders during the last week of treatment was 598 mg/day for monotherapy and 584 mg/day as combination therapy, with most responders receiving doses within the range 400–800 mg/day.

Conclusions: Quetiapine is effective and well tolerated over a wide dose range (up to 800 mg/day) with a target dose of approximately 600 mg/day. The tolerability of quetiapine was no different from its known profile in patients with schizophrenia.

Funding Source(s): AstraZeneca, Wilmington, Delaware, USA

References:

NR407  Tuesday, May 4, 12:00 p.m.—2:00 p.m.
Effects of Mood Stabilizers on Relapse and Recurrence in Bipolar Disorder
Supported by GlaxoSmithKline

Joseph F. Goldberg, M.D., Department of Psychiatry, Zucker Hillside Hospital, 79-59 263rd Street, Glen Oaks, NY 11004; Terence A. Ketter, M.D., Joseph R. Calabrese, M.D., Trisha Suppes, M.D., Mark A. Frye, M.D., Robin White, M.S.

Educational Objectives:
- At the conclusion of this presentation, the audience will have an understanding of the relative contributions of relapse vs. recurrence prevention in the therapeutic effects of lithium or lamotrigine.

Summary:
Introduction: Recently completed maintenance studies have demonstrated the efficacy of both lithium and the anticonvulsant mood stabilizer, lamotrigine, in delaying subsequent mood episodes in both recently depressed (GW605) or manic/hypomanic/mixed (GW606) bipolar outpatients.

Objective: This analysis examined whether these treatments reduced relapses, recurrence or both.

Methods: 588 currently or recently symptomatic bipolar I patients (DSM-IV) were randomized to 18 months of double-blind monotherapy with lamotrigine (100–400 mg/day), lithium (0.8–1.1 mEq) or placebo. Efficacy outcomes (time from randomization within the first week and onward, as monotherapy or in combination with lithium or divalproex. The average quetiapine dose in responders during the last week of treatment was 598 mg/day for monotherapy and 584 mg/day as combination therapy, with most responders receiving doses within the range 400–800 mg/day.

Conclusions: Quetiapine is effective and well tolerated over a wide dose range (up to 800 mg/day) with a target dose of approximately 600 mg/day. The tolerability of quetiapine was no different from its known profile in patients with schizophrenia.

Funding Source(s): AstraZeneca, Wilmington, Delaware, USA

References:

NR408  Tuesday, May 4, 12:00 p.m.—2:00 p.m.
Preliminary Experience With Levetiracetam in Bipolar Hypomania
Supported by UCB Pharma

Joseph F. Goldberg, M.D., Department of Psychiatry, Zucker Hillside Hospital, 79-59 263rd Street, Glen Oaks, NY 11004; Katherine E. Burdick, Ph.D.

Educational Objectives:
- At the conclusion of this session, the participant should be able to inform participants about new initial observations regarding the safety and effectiveness of the novel anticonvulsant levetiracetam for bipolar disorder.

Summary:
Background: Preclinical studies suggest that the novel N-type calcium channel blocker levetiracetam may possess antimanic and/or anxiolytic properties via its indirect GABAergic effects through allosteric modulation of GABA-A and glycine receptors. To date, little empirical investigation exists regarding its possible psychotropic properties.

Method: An initial case series of five DSM-IV bipolar outpatients with hypomanic features that were poorly responsive to standard pharmacotherapies received open-label monotherapy (n=4) or add-on therapy (n=1) with levetiracetam for up to six weeks.

Results: Significant reductions were observed in Young Mania Rating Scale (YMRS) scores from baseline (mean ± SD = 22 ± 5) to study end (mean ± SD = 9 ± 9) (Z=2.023, p=.043), while reductions in global severity (measured by CGI) were near-significant (p=.059). No significant changes were seen in depressive symptoms as measured by the Hamilton Depression Scale (HAM-D). Levetiracetam was generally well-tolerated and no exacerbations of mania or inductions or psychosis or agitation were encountered.

Conclusion: These preliminary findings suggest that levetiracetam may have value for hypomanic symptoms in bipolar patients. Controlled trials of levetiracetam in bipolar disorder are needed to affirm and extend these initial observations.

References:

NR409  Tuesday, May 4, 12:00 p.m.—2:00 p.m.
Pharmacokinetics/Dynamics of Continuous Versus Pulsatile Methylphenidate Treatment
Supported by Copley Pharmaceuticals

Ann M. Polcari, R.N., Department of Psychiatry, McLean Hospital, 115 Mill Street, Belmont, MA 02478; Martin H. Teicher, M.D., Mary Foley, M.S., Elizabeth Valente, M.A., Cynthia McGreener, Kamil Midha, Ph.D., Gordon McKay, Ph.D.
Educational Objectives:
At the conclusion of this session, the participant should be able to recognize that the efficacy of methylphenidate treatment for ADHD symptoms is effected by the drug delivery strategy.

Summary:
Recent studies indicate that the sustained efficacy of methylphenidate depends on pharmacokinetics, and that constant blood levels produce rapid tolerance and waning benefits. To overcome this problem methylphenidate preparations need to be pulsatile with periods of falling levels to restore sensitivity, or need to produce constantly increasing blood levels to surmount an underlying emerging tolerance. We reasoned that pulsatile delivery would minimize development of tolerance and produce greater efficacy at moderate doses than continuously increasing delivery. Forty-eight boys (10.6±1.1 yr) with ADHD combined subtype, who were all methylphenidate responsive, were randomly assigned to one of the four groups. Each subject received a total dose of 1 mg/kg/day methylphenidate administered to produce either pulsatile kinetics, steady-state blood levels, or a bolus + rising blood level pattern similar to Concerta™. Subjects had blood drawn for d-methylphenidate levels and computer testing for attention and hyperactivity (infrared motion analysis) at hourly intervals over the course of 12 hours. Methylphenidate exerted effects on attention and activity that correlated strongly with d-methylphenidate levels. A pulsatile tid pattern (0.4, 0.4 and 0.2 mg/kg) produced maximal peak and overall benefits on activity and attention. Continuously increasing regimens may require higher total doses to produce comparable benefits.

Supported in part by Copley Pharmaceuticals

References:

NR410 Tuesday, May 4, 12:00 p.m.—2:00 p.m.
Neuroprotective Properties of Quetiapine: A Potential Role in the Treatment of Neurodegenerative Disorders?
Supported by AstraZeneca Pharmaceuticals

Andrius Baskys, M.D., Mental Health, VA Health Care Systems, 5901 East 7th Street, 06/116A, Long Beach, CA 90822; Liwei Fang, B.S.C., Ildar Bayazitov, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to: (1) describe how organotypic hippocampal cell cultures can be used to study neurodegeneration; (2) summarize how the concentration of quetiapine and the timing of use affect experimentally induced cell death; (3) compare the neuroprotective effects of quetiapine with the effects of the NMDA blocker MK801.

Summary:
Objective: Progressive neurodegeneration may be responsible for emergence of dementia in patients with Parkinson's disease, and systemic analysis of neuroprotective properties of psychotropic drugs should provide a rationale for clinical studies. Since antipsychotic quetiapine is often used in dementia-associated psychoses, we studied its effects on neuronal survival.

Methods: To induce cell death, organotypic hippocampal cultures from 7-day-old Wistar rats were exposed to 50 M N-methyl-D-aspartate (NMDA) for 30 minutes or oxygen-glucose deprivation (OGD) for 60 to 120 minutes. Cell death was measured as propidium iodide uptake 24 and 72 hours after exposure and verified with Hoechst staining. Quetiapine (1 μM-100 μM) was added to the medium before NMDA/OGD, during NMDA/OGD or immediately after NMDA/OGD.

Results: Prolonged (24 hour-7 day) pretreatment with quetiapine significantly (P<0.05) and dose-dependently reduced NMDA-induced cell death at 1–100 nM concentrations. Unlike NMDA antagonist MK801, quetiapine was ineffective if applied together with NMDA, suggesting NMDA-independent mechanism. Quetiapine (10 nM) also reduced OGD dependent cell death.

Conclusion: Quetiapine is neuroprotective in NMDA- and OGD-induced cell death models. This property may contribute to its efficacy in treating psychosis of dementia and should be investigated clinically.

Supported by an investigator-initiated research grant from AstraZeneca Pharmaceuticals LP and VISN21 MIRECC to AR

References:

NR411 Tuesday, May 4, 12:00 p.m.—2:00 p.m.
NMS Diagnosis by DSM-IV and by Caroff
Zachias Cernovsky, Ph.D., Department of Psychiatry, University of Western Ontario, 98 Greenbrier Crescent, London, ON N6J 3X9, Canada; Varadaraj R. Velamoor, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to discuss the differences between DSM-4 and Caroff's system for NMS detection.

Summary:
Introduction/Hypothesis: The two leading systems for NMS detection are the one specified by DSM-4 and the one proposed by Caroff et al. (1991). Their statistical relationships were explored in our study.

Methods: Data from a national survey of 233 suspected NMS cases (age from 12 months to 90 years, mean = 40.8 years, SD=17.9) were analyzed to examine the relationships of the two diagnostic systems, and also their relationships to vital signs (BP, pulse, temperature), laboratory measures (Creatine Kinase, WBC, PH, P-O2, P-CO2), and ratings of behavioral symptoms (rigidity, dysphagia, agitation, coma, etc.).

Results: 83.7% patients with suspected NMS met DSM-4 criteria for NMS and only 33.9% met those required by Caroff. All those diagnosed so by Caroff were also classified so by DSM-4. Muscular rigidity correlated more closely with NMS by DSM-4 (phi=.75) than with Caroff's system (phi=.24). Abnormalities of BP and tachypnea/hypoxia correlated more closely with Caroff's system (phi=.38 and .34) than with DSM4 (phi=.17 and .16). The differences between the respective pairs of correlation coefficients are statistically significant.

Conclusions: The DSM-4 classified more patients as NMS than Caroff's system.

References:

NR412 Tuesday, May 4, 12:00 p.m.—2:00 p.m.
Quetiapine Reduces Cortisol-Excretion in Health Subjects Under an Acoustic Stress Condition Supported by AstraZeneca Pharmaceuticals
Stefan Cohrs, M.D., Psychiatry Department, University of Goettingen, Von Sieboldstrasse 5, Goettingen 37075, Germany; Kathrin Pohllmann, Zhenghua Guan, Wolfgan Jordan, M.D.; Gerald Huether, M.D., Eckart A. Ruether, M.D., Andrea Rodenbeck, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should better understand the effects of the atypical antipsychotic quetiapine on cortisol-excretion in healthy subjects, the implication for further research, and the possible use in different patient groups.

Summary:
Objective: The aim of this study was to investigate noninvasively the effects of quetiapine on HPA-axis activity in healthy male subjects.

Method: This double-blind, placebo-controlled, randomized cross-over study examined the excretion of overnight urinary cortisol as part of a larger study investigating the effects of quetiapine 25 mg and 100 mg in comparison to placebo given to 18 healthy male subjects under standard sleep laboratory conditions (N1) and acoustic stress (N2). A complete data set for urinary cortisol was available for 13 subjects.

Results: ANOVA showed a significant (p<0.01) effect for N1 vs. N2 with elevated total amount of cortisol excretion after acoustic stress. Quetiapine 25 mg and 100 mg significantly (p<0.001) reduced total amount of cortisol excretion and urinary cortisol concentration (p<0.0001) in comparison to placebo.

Conclusions: Acute administration of low doses of quetiapine is associated with a down-regulation of the HPA-axis in healthy subjects. This down-regulation of the HPA-axis may be an important aspect in quetiapine’s mode of action in patients.

The study was supported by AstraZeneca, D. We thank AstraZeneca for the supply of medication.

References:

NR413 Tuesday, May 4, 12:00 p.m.—2:00 p.m.
Fluoxetine in Men With a History of Partner Abuse Supported by Eli Lilly and Company
Emil F. Coccaro, M.D., Department of Psychiatry, University of Chicago, 5841 South Maryland Avenue, MC#3077, Chicago, IL 60637

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize that treatment with SSRIs may not be efficacious in men with history of partner abuse.

Summary:
Objective: To determine the efficacy of treating aggressive behavior in men with history of partner abuse.

Methods: 26 men with a recent history of aggressive partner abusing behavior entered a randomized, placebo-controlled, trial of fluoxetine (20 to 60 mg po qd). The primary outcome measure was the Aggression Score from the OAS-M. Results: Fluoxetine-treated subjects (n = 13) did not differ from placebo-treated subjects (n = 13) on any key demographic or behavioral variables. While a significant "pre-post" reduction in OAS-M Aggression Score was noted in placebo-treated subjects (t(2) = 2.336, p = .038), fluoxetine-treated subjects showed no such reduction in OAS-M Aggression scores (t(11) = 1.032, p = .322). Overall, no drug-placebo differences for OAS-M Aggression Score were seen in any analysis (e.g., LOCF Analysis: ANCOVA F(1,25) = .196, p = .662).

Conclusions: Despite the small sample, these results do not support the hypothesis that treatment with an SSRI is associated with a reduction in aggressive behavior among men with a recent history of partner abusing behavior. Reasons for this negative finding will be discussed.

Supported by NIMH: R01 MH054804 and Lilly Research Laboratories.

Funding Source(s): NIMH & Lilly Res. Labs.

References:

NR414 Tuesday, May 4, 12:00 p.m.—2:00 p.m.
Pharmacokinetics of Lamotrigine and Oxcarbazepine Cotherapy Supported by GlaxoSmithKline
John A. Ascher, M.D., Psychiatry Department, GlaxoSmithKline, 5 Moore Drive, Room 17.1356.IC, Research Triangle, NC 27709; Jochen Theis, M.D., Jagdev Sidhu, Ph.D., Sarah Job, M.S.C., Joanne Palmer, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to understand the pharmacokinetic effects of co-therapy with lamotrigine and oxcarbazepine.

Summary:
Introduction: In vitro, oxcarbazepine (OXC) and its metabolite 10-monohydroxy (MHD) are weak inducers of UDP-glucuronyl transferase, which may increase lamotrigine (LTG) conjugation. Objective: We investigated the pharmacokinetics (PK) and tolerability of the combination of LTG and OXC in healthy volunteers.

Methods: 47 healthy, non-smoking, adult males were randomized to receive LTG (titrated to 200mg/day) or placebo (PBO) on days 1–53. OXC (titrated to 600 mg bd) or PBO were added on days 43–53 resulting in 3 parallel cohorts receiving the combinations of LTG+OXC, LTG+PBO or OXC+PBO. PK profiles were obtained at steady state.

Results: AUC(0-24) and C( max) of LTG, OXC and its active metabolite MHD were not significantly affected by cotherapy; all were on average less than 10% lower compared with monotherapy. Adverse events (AEs) were reported more frequently with OXC+LTG than with either monotherapy. The most common AEs were headache, dizziness, nausea, and somnolence.
Conclusions: Co-administration of LTG and OXC does not affect the PK of either drug. The PK results support co-administration in patients who may benefit from combination therapy.

References:

NR415 Tuesday, May 4, 12:00 p.m.–2:00 p.m.
A Pharmacokinetic Interaction Study of Lamotrigine and Olanzapine
Supported by GlaxoSmithKline

John A. Ascher, M.D., Psychiatry Department, GlaxoSmithKline, 5 Moore Drive, Room 17.1356.1C, Research Triangle, NC 27709; Jagdev Sidhu, Ph.D., Sarah Job, M.S.C., Jochen Theis, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to understand the pharmacokinetic effects of co-therapy with lamotrigine and olanzapine.

Summary:
Introduction: Co-therapy with antipsychotics and antiepileptics is becoming increasingly common in bipolar disorder.
Objective: To examine the pharmacokinetic interactions of olanzapine (OLZ) added to lamotrigine (LTG) in healthy volunteers.
Methods: 52 non-smoking males (age 18–55 years) were randomized to LTG (titrated to 200mg/day) or placebo (PBO). OLZ (titrated to 15 mg) or PBO were added on days 43–56 resulting in three parallel cohorts receiving the combination of LTG+OLZ (n=16), LTG+PBO (n=12) or OLZ+PBO (n=18) for 2 weeks. Serum blood levels, adverse events (AEs), and blood chemistry were examined. Pharmacokinetic profiles were obtained at steady state.
Results: LTG AUC₀₋₂₄ and Cmax were, on average, 24% and 20% lower with LTG+OLZ compared with LTG+PBO, respectively. OLZ AUC₀₋₂₄ and Cmax were comparable with OLZ+LTG and OLZ monotherapy. AEs were similar with LTG+OLZ and OLZ+PBO; fewer AEs were reported with LTG+PBO. The most common AEs were transaminase elevations, fatigue, and dizziness. Transaminase elevations and dizziness were reported at similar frequencies with LTG+OLZ and OLZ+PBO, but not with LTG+PBO.
Conclusions: The combination of OLZ and LTG was well-tolerated, with the type, frequency, and severity of adverse events similar to lamotrigine monotherapy. These results support co-administration in patients who may benefit from combination therapy.

References:

NR416 Tuesday, May 4, 12:00 p.m.–2:00 p.m.
Double-Blind, Placebo-Controlled Trial of Sibutramine for Olanzapine-Associated Weight Gain Supported by Eli Lilly and Company

David C. Henderson, M.D., Department of Psychiatry, Massachusetts General Hospital, 25 Staniford Street, Boston, MA 02114; Dana Nguyen, M.A., Tara B. Daley, M.P.H., Pearl Louie, M.D., Christina Burba, M.P.H., Paul Copeland, M.D.

Educational Objectives:
At the conclusion of this session, participants should be able to understand the safety and efficacy of sibutramine for weight loss in olanzapine-treated patients.

Summary:
Objective: Olanzapine has been shown to be an effective and generally well-tolerated antipsychotic medication in the treatment of schizophrenia. Weight gain is a commonly observed side effect of olanzapine. This study examined the effectiveness of sibutramine, an FDA approved agent for weight loss, in overweight and obese subjects treated with olanzapine.
Method: Subjects included 43 adults with a diagnosis of schizophrenia or schizoaffective disorder, on a stable dose of olanzapine, and had a body mass index (BMI) >30 kg/m² or ≥27 kg/m² with cardiovascular risk factors. In a double-blind, randomized, placebo-controlled study, subjects received 12 weeks of placebo or sibutramine (up to 15 mg/day) and participated in a weekly nutrition and behavioral modification group for eight weeks.
Results: Forty-three subjects signed informed consent and 37 were randomized. For the placebo group, the mean age was 40.7 ± 9.9 years with 61% male (n=11), 67% Caucasian and 28% African American. For the sibutramine group, the mean age was 43.2 ± 10.6 years, with 63% male, 68% Caucasian and 26% African American. There were no differences on demographic and baseline values (weight, BMI and blood pressure). There was a significant difference in body weight (lbs) comparing the two groups from baseline to week twelve (P < .05), with the sibutramine group showing significant weight loss (mean loss of 15 lbs by week twelve for sibutramine group). There was a significant difference, at week 12, comparing groups in waist circumference (P < .005) and BMI (P < .001) with the sibutramine-treated group showed a significant reduction in both measures compared to baseline. Finally, the sibutramine group had significantly lower hemoglobin A1C than the placebo group at week twelve (P < .05). There were no significant differences between groups on any side effects; though the sibutramine treated group exhibited a 3.5 mmHg increase in systolic blood pressure at week twelve.
Conclusions: Sibutramine was an effective and well-tolerated weight loss agent when used as an adjunct to behavior modification in patients with schizophrenia and schizoaffective disorder being treated with olanzapine.
Funding Source(s): NARSAD Young Investigator Award (Dr. Henderson), and an Investigator-initiated Independent Research Grant from Eli Lilly and Co

References:
NR417  Tuesday, May 4, 12:00 p.m.–2:00 p.m.

Glucose Metabolism in Patients With Schizophrenia Treated With Atypical Antipsychotics

Supported by Janssen Pharmaceutica and Research Foundation

David C. Henderson, M.D., Department of Psychiatry, Massachusetts General Hospital, 25 Stanford Street, Boston, MA 02114; Tara B. Daley, M.P.H., Enrico Cagliero, M.D., Christina Burba, M.P.H., Paul Copeland, M.D., Eden A. Evins, M.D., Donald C. Guff, M.D.

Educational Objectives:

At the conclusion of this session, participants should be able to understand the degree to which different antipsychotic medications (olanzapine, clozapine, risperidone) affect glucose effectiveness and utilization and insulin resistance.

Summary:

Objective: The incidence of new-onset diabetes mellitus (DM) appears to be increasing in schizophrenia patients treated with certain atypical antipsychotic agents. It is unclear whether the atypical agents are directly affecting glucose metabolism or simply increasing known risk factors for diabetes, such as obesity, lipid abnormalities, and decreased activity secondary to sedative effects. This study examines the two drugs most clearly implicated (clozapine and olanzapine) and the atypical agent least implicated (risperidone) using a frequent sampled intravenous glucose tolerance test (FSIVGTT).

Methods: A cross-sectional design was conducted in stable, treated schizophrenia patients evaluated using a FSIVGTT and Bergman’s Minimal Model Analysis. Thirty-six nonobese (body mass index [BMI], <30 kg/m²) subjects with schizophrenia or schizoaffective disorder were studied. Subjects were matched by BMI, and treated with mono-antipsychotic agent therapy with either clozapine, olanzapine, or risperidone.

Results: Fasting serum insulin concentrations differed between groups (p=.047) with significant differences between both clozapine and risperidone (p=.027) and olanzapine and risperidone (p=.039). There was a significant difference in insulin sensitivity index (SI) between groups (p=.0003) with clozapine and olanzapine subjects exhibiting significant insulin resistance compared to risperidone-treated subjects: clozapine vs. risperidone (p=.0001); olanzapine vs. risperidone (p=.01). Insulin resistance calculated by the HOMA-IR also differed significantly between groups (p=.014); clozapine vs. risperidone (p=.006) olanzapine vs. risperidone (p=.02). Both clozapine and olanzapine showed elevations in HOMA-IR compared to risperidone. There was a significant group effect difference in SG (p=.025) and between groups comparing clozapine to risperidone (p=.015) and olanzapine to risperidone (p=.026).

Conclusions: As a group, both non-obese clozapine- and olanzapine-treated subjects displayed significant insulin resistance and impairment of glucose effectiveness and utilization, compared to risperidone-treated subjects.

Funding Source(s): National Institute of Health (NIH/NCCR) Grant 5MO1RR01066-24 (General Clinical Research Center, Dr. Nathan), NARSAD Young Investigator Award (Dr. Henderson), and an Investigator-initiated independent Research Grant from Janssen Pharmaceutica

References:


NR418  Tuesday, May 4, 12:00 p.m.–2:00 p.m.

Clozapine and Cardiovascular Risks: Ten-Year Estimates

David C. Henderson, M.D., Department of Psychiatry, Massachusetts General Hospital, 25 Stanford Street, Boston, MA 02114; Pearl Louie, M.D., Tara B. Daley, M.P.H., Dana Nguyen, M.A., Laura J. Kunkel, M.D., Elizabeth Salib, Pamposh Koul, B.S.

Educational Objectives:

At the conclusion of this session, the participant should become aware of the increase in cardiovascular risk factors after initiating clozapine treatment and to monitor and counsel patients on risk reduction.

Summary:

Objective: This study examined the change in risk factors for cardiovascular disease in clozapine-treated subjects, after clozapine initiation, over a ten-year period. Data from 97 schizophrenia patients treated with clozapine were examined for cardiovascular risk using known risk factors such as age, body mass index (BMI), systolic and diastolic blood pressure, diabetes, history of cardiovascular or cerebrovascular disease, serum total cholesterol, and smoking status.

Methods: Seventy (72%) were men and 27 (28%) were women. The mean age at clozapine-initiation was 36.40 +/- 7.79 years for men and 36.93 +/- 8.41 years for women and four African Americans (4%), three Hispanic (3%) and one Asian (1%).

Results: Preliminary analysis showed a significant increase in cardiovascular risk factors at six months and one year following clozapine initiation (t=25.07, p=0.0001). Both men and women showed a significant increase in risk (p=.0001). While men began clozapine with the same relative risks as age matched men in the general population, they more than quadrupled their risk over the first five years of treatment. Overall, there were five deaths from cardiovascular disease (including two individuals less than 30 years old) along with four nonfatal myocardial infarctions and one stroke. Kaplan-Meier survival estimate for ten year mortality from cardiovascular disease in clozapine-treated patients was 10%.

Conclusion: Long-term treatment with clozapine may significantly increase the risk of death from cardiovascular disease with estimates of up to 10% of clozapine-treated patients will die from cardiovascular disease in a ten-year period. Clinicians must be aware of the risks of cardiovascular disease in clozapine-treated patients and monitored and counsel patients on risk reduction.

References:


NR419  Tuesday, May 4, 12:00 p.m.–2:00 p.m.

The Complex Relationship Between SSRI Side Effects and Discontinuation

Supported by Merck & Co., Inc.

Stephen B. Woolley, M.P.H., Burlingame, Institute of Living, 2200 Retreat Avenue, Hartford, CT 06106; John W. Goethe, M.D., Brenda Woznicki, B.S., Kathy Foley, Ph.D., X. Henry Hu, M.D.
NR421  Tuesday, May 4, 12:00 p.m.—2:00 p.m.
Bone-Mineral Density in Women With Antipsychotic-Induced Amenorrhea
Supported by AstraZeneca Pharmaceuticals
Angelika Wieck, M.D., Psychiatry Department, Wythenshawe Hospital, Southmoor Road, Manchester M23 9LT, United Kingdom; Ben Akande, M.D., Peter M. Haddad, M.D., Judith Adams, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize: (1) that antipsychotic-induced amenorrhea of relatively short duration is associated with significant bone loss; (2) that the bone loss affects mostly trabecular bone.

Summary:
Introduction: During treatment with prolactin-elevating antipsychotics about 50% of premenopausal women develop menstrual irregularities and estrogen-deficiency. In non-psychiatric populations estrogen deficiency is associated with bone loss.

Methods: Inclusion criteria were antipsychotic-induced amenorrhea (> 12 months), hyperprolactinaemia, no steroid therapy and Caucasian origin. BMD was measured using quantitative CT (QCT) (left radius) and DXA (spine, left hip). A one-sample t-test was used to compare (age-adjusted) Z-scores with normative BMD data.

Results: 13 women were included (mean age: 36.5 (9.6) years, median duration of amenorrhea: 15 months, mean BMI: 30.2 (7.8)). Mean prolactin levels were 1479.8 (SD 962.1) mU/L. Serum concentrations of ovarian hormones, LH and FSH confirmed anovulatory status. BMD was highly significantly reduced in trabecular bone of the radius (mean Z-score: -0.66, p<.000) but not at other bone sites. The finding was not due to exercise levels, smoking or other confounding variables.

Conclusion: Women with antipsychotic-induced amenorrhea have significantly decreased BMD in the trabecular bone of the radius. The absence of effects on other bone sites may be explained by the relatively short duration of hypoestrogenism, the high sensitivity of trabecular bone to estrogen deficiency and the superiority of quantitative CT measurements compared to dual X-ray absorptiometry.

References:
NR422  Tuesday, May 4, 12:00 p.m.–2:00 p.m.
Dextromethorphan-Potential Interaction With Methylphenidate or Atomoxetine
Supported by McNeil Pharmaceuticals
Lois M. Jessen, Pharm.D., Pharmacy Department, Rutgers University, 160 Frelinghuysen Road, Busch Campus, Piscataway, NJ 08854-8020; Kris Ramabadrnan, Ph.D., Patrick E. Ciccone, M.D., Steven A. Silber, M.D., Debra L. Bowen, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to identify the potential for drug-drug interactions between dextromethorphan and the ADHD medications methylphenidate and atomoxetine.

Summary:
Objective: Dextromethorphan, a common ingredient in cough suppressant preparations, is metabolized through the P450 pathway. This good laboratory practice study assessed whether dextromethorphan could affect the in vitro metabolism of methylphenidate and/or atomoxetine.

Methods: Incubations of dextromethorphan with and without effector were performed using pooled human liver and recombinant cytochrome P450 2D6 (CYP2D6)-containing microsomes. Atomoxetine and d-threomethylphenidate concentrations of 0.1, 1, and 10 times the reported therapeutic concentrations were tested. Paroxetine was included as a reference, and quinidine was used as a positive control inhibitor. Changes in substrate metabolism were assessed to indicate in vitro CYP2D6-mediated interactions.

Results: Atomoxetine and paroxetine inhibited the formation of the CYP2D6-specific metabolite of dextromethorphan, dextrorphan, by >50% in human liver microsomes and by >80% in recombinant microsomes. Conversely, dextromethorphan and dextrorphan modestly inhibited atomoxetine and paroxetine metabolism. d-Methylphenidate did not inhibit dextrorphan formation in either microsome preparation, and d-Methylphenidate metabolism was unaffected by dextromethorphan or dextrorphan.

Conclusion: Based on these in vitro results, there appears to be potential for in vivo interaction between dextromethorphan and atomoxetine or paroxetine in patients with ADHD. However, in vitro evidence does not support the plausibility of an in vivo interaction between dextromethorphan and d-Methylphenidate.

Study supported by McNeil Consumer & Specialty Pharmaceuticals

References:
1. Yu A, Haining RL: Comparative contribution to dextromethorphan metabolism by cytochrome P450 isoforms in vitro: can dextromethorphan be used as a dual probe for both CYP2D6 and CYP3A activities? Drug Metab Dispos 2001; 29:1514–1520.

NR424  WITHDRAWN

NR425  Tuesday, May 4, 12:00 p.m.–2:00 p.m.
Brain Injury, APOT-E4, and Cognition in the Elderly: One-Year Outcome
Andrea Phillips, B.A., Psychiatry Department, University of Toronto, FG22-2075 Bayview Avenue, Toronto, ON M4N 3M5, Canada; Prathiba Shammi, Ph.D., Anthony Feinstein, M.D., Marciano Reis, M.D., Mark J. Rapoport, M.D.

Educational Objectives:
At the conclusion of this session, the participant should understand the impact of a mild-to-moderate traumatic brain injury on cognition one year after injury, and the potential mediating role of genetics.
Objective: To explore the effects of mild-to-moderate traumatic brain injury (TBI) and Apolipoprotein E-ε4 (APOE-ε4) on cognition in older adults. Epidemiological studies have shown links between remote TBI, the ε4 allele, and the later development of dementia, but there are no prospective studies to date investigating this relationship in patients who sustain a TBI in older age.

Methods: Participants with acute mild-to-moderate TBI were compared with age-, gender-, and education-matched controls on aspects of cognition. APOE genotype was determined. Neuropsychological tests of attention, memory, language, and executive functioning were administered in the first year of a two-year longitudinal study. Logistic regression was conducted of effects of age, TBI, APOE, education, and medical illness on cognition.

Results: Forty-one subjects aged fifty and over (mean age 66.9 years, SD 8.26) and fifty-four matched controls were assessed. There were no significant demographic or APOE differences between cases and controls. TBI was associated with executive dysfunction (t=3.38, p<0.001), but TBI, APOE, and their interactions did not predict other test scores one year post-injury.

Conclusion: Mild-to-moderate TBI was associated with executive dysfunction one year after injury in older patients, in the absence of other significant cognitive differences. The APOE-ε4 allele did not alter this relationship.

Funding Source(s): Ontario Neurotrauma Foundation

References:

NR426 Tuesday, May 4, 12:00 p.m.–2:00 p.m.
Convergent Validity of the Neurological Disorders Depression Inventory in Epilepsy
Supported by GlaxoSmithKline

John Barry, M.D., Department of Psychiatry, Stanford University, 401 Quarry Road, MC 5723, Stanford, CA 94305; Frank Gilliam, M.D., Kimford J. Meador, M.D., Bruce Hermann, J. Mitchell Miller, Pharm.D., Andres M. Kanner, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize that compared with normals, bipolar patients have persistent neuropsychological deficits even during periods of euthymia.

Summary:
Objective: To evaluate the convergent validity between a new self-report depression screening questionnaire for patients with epilepsy and the Beck Depression Inventory (BDI-II) following drug therapy.

Background: The BDI-II is a self-report measure of depression in which scores ≥ 18 indicate a moderate to severe depression. The 6-item Neurological Disorders Depression Inventory in Epilepsy (NDDI-E) has been validated against the Structured Clinical Interview for DSM-IV Axis 1 Disorders (SCID 1-research version) with scores of ≥15 indicating a likely moderate-severe depression. It is expected that these psychometric tools measure comparable levels of depression and would respond to effective treatment in a similar fashion.

Methods: One hundred fifty-nine patients with epilepsy enrolled in a 36-week open-label trial evaluating mood changes after lomotrigine adjunctive therapy to a stable anti-epileptic drug treatment. Mood changes were measured by self-report scores on the NDDI-E and BDI-II. Preliminary results are reported.

Results: A total of 36 patients have completed the 19 week adjunctive phase of the protocol to date. Mean BDI-II and NDDI-E scores were 20.0 and 14.1 respectively at screen and 12.3 for both instruments at Week 19. The effect size was 0.6 for the BDI-II and 0.4 for NDDI-E. Between baseline and Week 19, the mean decrease in BDI-II score was 7.75 (p=0.0001) and the mean decrease in NDDI-E score was 1.86 (p<0.01). Spearman Correlation was 0.645 (p<0.0001)

Conclusion: This study provides evidence for convergent validity between the NDDI-E and the BDI-II.

Funding Source(s): Funded by a research grant from GlaxoSmithKline

References:

NR427 Tuesday, May 4, 12:00 p.m.–2:00 p.m.
Neuropsychological Deficit in Euthymic Patients Suffering From Bipolar Disorder
Judith Jaeger, Ph.D., Cenorr Department, Zucker Hillside Hospital, 75-59 263rd Street, Glen Oaks, NY 11004; Stephanie Berns, Ph.D., Rebecca Iannuzzo, Ph.D., Sara Davis-Conway, M.A., Sarah Uzelac, M.A., Pam Derosse, M.A., Christina Gomes, B.A.

Educational Objectives:
At the conclusion of this session, the participant should recognize that compared with normals, bipolar patients have persistent neuropsychological deficits even during periods of euthymia.

Summary:
Objective: Studies suggest that neuropsychological (NP) deficits are present in bipolar disorder (BPD) during illness episodes and periods of euthymia. We report on interim findings from a longitudinal, naturalistic study of BPD.

Method: Consenting inpatients were given comprehensive NP and psychopathology batteries when stabilized following admission. Testing was repeated after discharge in 18 patients who achieved eight continuous weeks of euthymia (6 females, age=34.13 (s.d.=11.33), education=13.50 (2.62)). Patient data was also compared to 29 normal controls (16 males, age=27.20 (6.39), education=14.71 (1.37)). NP tests were selected based upon our previous work in schizophrenia (Jaeger, 2003). Alpha was adjusted to p<0.01 to correct for multiple comparisons.

Results: Between baseline assessment and euthymia follow-up, NP test performance changed very little. Of 25 measures considered, only three (indices of working memory and basic attention) showed significant change. When compared to normals highly significant differences were found—euthymic patients performed worse on all measures of verbal memory, verbal and performance IQ, as well as motor and information processing speed. None of the three measures that improved from baseline to euthymia were among those that distinguished euthymics from controls. 

Conclusion: These preliminary findings suggest the presence of distinct state and trait NP deficits in BPD.

Funding Source(s): NIMH FUNDED: RO1MH60904-0

NR428 Tuesday, May 4, 12:00 p.m.—2:00 p.m.
Olfactory Function in Euthymic Patients With Bipolar Disorder
Supported by AstraZeneca Pharmaceuticals
Stephanie Krueger, M.D., Psychiatry Department, Clarke Institute, 250 College Str, Toronto, ON M5T 1R8, Canada; Thomas Hummel, Johannes Frasnelli, M.D., Peter Braeunig, M.D.

Educational Objectives:
At the conclusion of this session, the participant should understand the functional anatomy of the olfactory cortex, understand the basics of olfactory testing, and learn about the relevance of this method to bipolar disorder.

Summary:
Background: Some patients with bipolar disorder (BD) experience mood episodes following emotional life events, while others do not. There is evidence that orbitofrontal hypoactivity may be related to this, as the orbitofrontal cortex is involved in the regulation of emotional responses and behaviour to external events. The close anatomical and functional connection between orbitofrontal cortex and olfactory processing suggests that patients with heightened emotional reactivity may exhibit altered olfactory function.

Method: Olfactory function was assessed in seven euthymic BD patients with a history of event-triggered episodes and in 9 euthymic BD patients without this history. Olfactory tests included event-related potentials, odor thresholds, odor identification, and odor discrimination.

Results: Odor thresholds were significantly lower in BD patients, with event-triggered episodes compared with the other BD group. In addition, patients with event-triggered episodes showed significantly shorter N1 peak latencies of the olfactory event-related potential. For latencies P2, patients with triggered episodes exhibited pronounced differences to left- or right-sided stimulation, while there was little difference for the other patient group.

Conclusions: The findings indicate a disinhibition of orbitofrontal areas involved in the processing of external emotional events and olfactory function. Olfactory function tests may be used as a screening method to separate patients at risk for emotionally triggered episodes.

Funding Source(s): GERMAN RESEARCH SOCIETY (DFG)

References:
The Telefactor EEG monitoring device in the EEG recording room did not yield any statistically significant difference. We examined the right-left asymmetries of the endocrine measures. There were no statistically significant differences between the groups.

**Conclusions:** The examination of right-left asymmetries did not yield any statistically significant difference.

**References:**

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**NR431**  
Tuesday, May 4, 12:00 p.m.–2:00 p.m.  
**Immune and Neuroendocrine Changes in PTSD Treatment With SSRIs and Placebo**  
Supported by Forest Laboratories, Inc.

Phoebe M. Tucker, M.D., Psychiatry Department, University of Oklahoma Health Science, 920 Stanton L. Young Boulevard, WP3440, Oklahoma City, OK 73104; Shehzad Niazi, M.D., Donald Parker, Ph.D., Dorothy Wyatt, R.N., Christie Burgin, Ph.D., Akh Hossain, M.D., Christie Thompson

**Educational Objectives:**  
At the conclusion of this session, the participant will understand inter-related roles of cytokines and cortisol relevant to studies of PTSD patients, and how treatment may affect these immune and endocrine measures.

**Summary:**  
*Objective:* To assess prospectively effects of PTSD treatment with SSRI’s and placebo on emotional symptoms and measures of cortisol and interleukin. This study explores the reciprocal influences of the nervous, immune and endocrine systems in the pathophysiology of PTSD.

*Method:* 58 adult outpatients with chronic PTSD by SCID and 21 healthy controls had baseline assessments of PTSD (CAPS), depression (BDI), salivary 8am and 4pm cortisolos and serum interleukin 1-B and interleukin 2-R. PTSD subjects completed double-blind, ten-week treatment with citalopram (n=19), sertraline (n=18) and placebo (n=7), with psychometric, immune and endocrine measures repeated.

**Results:** PTSD patients had higher baseline PTSD, depression and interleukin 1-B and 2-R levels than controls (p < 0.0001), but did not differ in am or pm cortisolos. All treatment groups improved significantly in PTSD and depressive symptoms (p < 0.05). Cortisol levels were unchanged with SSRI treatment, while pm cortisol increased significantly in the placebo group (p = 0.03).

**Conclusions:** Cytokines may be sensitive biological markers for improvement in PTSD, both with SSRI and placebo treatment. Although interleukin 1-B and interleukin 2-R can stimulate cortisol production, lowered cytokines after PTSD treatment was not associated with changes in cortisol in SSRI groups. Possible implications of cytokines changes may include effects on immune functioning, sleep and stress sensitivity.

**Funding Source(s):** Forest Pharmaceuticals, Inc.

**References:**

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**NR432**  
Tuesday, May 4, 12:00 p.m.–2:00 p.m.  
**Effects of Propofol Anesthesia on Seizure Duration**  
Okan Caliyurt, M.D., Department of Psychiatry, Trakya University, School of Medicine, Edime 22030, Turkey; Erdal Vardar, M.D., Cengiz Tuglu, M.D., Erkan Abay, M.D.

**Educational Objectives:**  
At the conclusion of this session, the participant should be aware of the possible effects of propofol and other anesthetics on ECT seizure duration.

**Summary:**  
*Objective:* Propofol is a widely used anesthetic agent that is associated with smaller hemodynamic response during ECT. Propofol is known to reduce electroconvulsive therapy (ECT) seizure duration (1:2). The aim of the present study was to compare ECT seizure durations in patients receiving propofol anesthesia and patients without anesthesia.

*Method:* In this retrospective study, seizure durations of the 15 patients who had propofol anesthesia and 11 patients who had ECT without anesthesia assessed. Patients selected consecutively, all the patients treated with same ECT device (Thymatron III DGx, Somatics Inc) and seizure duration measurements were based on the device automated seizure duration determinations.

**Results:** Both groups were similar in age and gender distribution. Mean seizure duration of the patients who recieved propofol anesthesia (44.38±14.52) was higher than patients who had no anesthesia (39.45±3.47). But this difference was not statistically significant (p=0.22).

**Conclusions:** Contrary to previous studies, there was no considerable effect of propofol on seizure duration found. Design of the study is different from other studies that they compares two different induction agents therefore this study gives more reliable results. Our results are contradictory but should be interpreted cautiously because of the small study group and larger standard deviation of the propofol group.

**References:**

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**NR433**  
Tuesday, May 4, 12:00 p.m.–2:00 p.m.  
**Biological and Behavioral Changes During Cholesterol-Lowering Therapy**  
Jan Vevera, M.D., SPH, University of California, Berkeley, 140 Warren Hall, MC 7380, Berkeley, CA 94720; Zdenek Fiser,
Ph.D., Tomas Kvasnicka, M.D., Zdenek Hanus, Lucie Starkerova, M.D., Richard Ceska, M.D., Hana Papezova, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize that decreasing cholesterol levels do not decrease, but increase serotonin uptake. The implication for clinician practice is that patients could be vulnerable to increased impulsiveness during the first two months of cholesterol lowering therapy.

Summary:

Introduction: A number of studies have reported an increased risk for violent deaths, suicide and depression at reduced serum cholesterol concentrations. Hypothesized links with the impairment of brain serotonin neurotransmission have not been satisfactorily tested.

Method: Serum and membrane cholesterol, microviscosity of erythrocyte membranes, platelet serotonin uptake and clinical parameters were determined in 18 controls and 17 persons with hypercholesterolemia before the first administration of simvastatin and after one month, two months and 13–16 months of treatment (9 patients only).

Results: Microviscosity of plasma membranes was increased in hypercholesterolemic patients compared to controls. Short-term treatment induced a decrease in serum and membrane cholesterol concentration, a decrease in membrane microviscosity and an increase in serotonin transporter activity (5HTT). However, long-term (13–16 months) therapy has a different effect on both membrane cholesterol and 5HTT activity which returned to the values before treatment. Impulsivity, depressiveness, and sensation seeking remain unchanged.

Conclusion: We did not confirm the hypothesis that decreases in cholesterol concentration causing the increased risk of violence or depression due to altered microviscosity of plasma membranes and consequential inhibition of serotonin transmission. On the other hand, normal or higher cholesterol concentrations might have a protective effect on depressive or impulsively violent persons.

Funding Source(s): NIH Fogharty and Ucberkeley D43 Two 5810; MSM 111100001; GAUK 27 12000C

References:


NR434 Tuesday, May 4, 3:00 p.m.-5:00 p.m.

A New Differential Diagnosis Proposal for ADHD: The Permeable Personality

Eduardo J. Barragan, M.D., Department of Neurology, Hospital Infantil Mexico, Dr Marquez No. 162, Mexico DF 06720, Mexico

Educational Objectives:

At the conclusion of this session, the participant should recognize a new approach in the diagnosis and outcome of pediatric patients with ADHD.

Summary:

Introduction: ADHD is the more common neuropsychiatric disorder diagnosis in childhood. The prevalence is uncertain, but estimates range between 3 and 15 worldwide. Its more common in boys than in girls (3:1). The diagnosis is clinical (DSM-IV) and response to psychoeducational stimuli very high. However, diagnostic labels for inattentive, impulsive, and innated children have changed numerous times over the last decades; and the difference seeing in develop course, high heterogeneity and pharmacological responses (even responding to non conventional treatments) may be due a different personality development and not a symptoms from nervous system disorder.

Methods: 410 children with symptoms of innatention, hyperactivity impulsivity, etc. were evaluated in a pediatric neurology department between 1999 and 2003. We examined the core symptoms: Conners test EEG activity and response to medications.

Results: 279 patients (68%) of the sample had criteria (DSMIV) for ADHD. Of these samples, 73% were boys, present academic achievement skills (45%), learning disabilities (18%) delayed onset of language disruptive classroom behavior, normal physical examination. 20% of the rest population show a problems in motor coordination (88%) delayed onset of language and speech impairments (83%), learning disabilities (92%), poor self-regulation of emotion, high sensibility high internalization of own behavior but problems with communication skills, noble, creative, problems in visuospatial performance and common neurological soft signs related to motor coordination and generalized hypotonia. These patients were a poor responders to psychoeducational, and had a frequent comorbility with anxiety disorders (90%).

Conclusions: The permeable personality is a proposal of a new differential diagnosis for ADHD patients who display differences in their development courses, need another strategies and pharmacological approaches and try to explain one of the pathways in these heterogenous group of patients.

References:


NR435 Tuesday, May 4, 3:00 p.m. -5:00 p.m.

Higher Impact of Psychoeducation Than Atypicals in the Treatment of Patients With Schizophrenia

Sergio A. Strejilevich, M.D., Salud Mental, Area Investigation, Congreso 2477 D, Buenos Aires 1429, Argentina; Eduardo A. Leiderman, M.D., Eduardo Padilla, M.D., Maria Calvo, M.D., Julian Bustin, M.D., Julieta Cassone, M.D., Ana Palatnik, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to discriminate the impact of psychoeducational and medication treatments in schizophrenics symptomatology.

Summary:

Objective: To assess quality of life and symptomatology in schizophrenic outpatients in naturalistic treatment conditions.

Methods: We analyzed the data of a multicentric study in four psychiatric centers in Argentina. A randomized sample of 69 schizophrenic patients was assessed and their relatives were surveyed. Symptoms, side effects, and quality-of-life scales were scored. Raters were blind to hypothesis. Thirty-one percent were medicated with neuroleptics, 45% with clozapine, and 20% with other atypical drugs. Mean dose of neuroleptics was 8.9 ± 5.8 mg haloperidol. Thirty-eight percent of relatives had received psychoeducational information.

Results: There were no differences in symptomatology and quality of life between patients medicated with atypicals or neuroleptics. On the other hand, patients whose relatives received psychoeducational information had significantly less PANSS general, CGI and Ham-D scores (PanssG.: 32.08 ± 6.8 Vs. 39.7 ± 10.4

NR434 Tuesday, May 4, 3:00 p.m.-5:00 p.m.

A New Differential Diagnosis Proposal for ADHD: The Permeable Personality

Eduardo J. Barragan, M.D., Department of Neurology, Hospital Infantil Mexico, Dr Marquez No. 162, Mexico DF 06720, Mexico

Educational Objectives:

At the conclusion of this session, the participant should recognize a new approach in the diagnosis and outcome of pediatric patients with ADHD.

Summary:

Introduction: ADHD is the more common neuropsychiatric disorder diagnosis in childhood. The prevalence is uncertain, but estimates range between 3 and 15 worldwide. Its more common in boys than in girls (3:1). The diagnosis is clinical (DSM-IV) and response to psychoeducational stimuli very high. However, diagnostic labels for inattentive, impulsive, and innated children have changed numerous times over the last decades; and the difference seeing in develop course, high heterogeneity and pharmacological responses (even responding to non conventional treatments) may be due a different personality development and not a symptoms from nervous system disorder.

Methods: 410 children with symptoms of innatention, hyperactivity impulsivity, etc. were evaluated in a pediatric neurology department between 1999 and 2003. We examined the core symptoms: Conners test EEG activity and response to medications.

Results: 279 patients (68%) of the sample had criteria (DSMIV) for ADHD. Of these samples, 73% were boys, present academic achievement skills (45%), learning disabilities (18%) delayed onset of language disruptive classroom behavior, normal physical examination. 20% of the rest population show a problems in motor coordination (88%) delayed onset of language and speech impairments (83%), learning disabilities (92%), poor self-regulation of emotion, high sensibility high internalization of own behavior but problems with communication skills, noble, creative, problems in visuospatial performance and common neurological soft signs related to motor coordination and generalized hypotonia. These patients were a poor responders to psychoeducational, and had a frequent comorbility with anxiety disorders (90%).

Conclusions: The permeable personality is a proposal of a new differential diagnosis for ADHD patients who display differences in their development courses, need another strategies and pharmacological approaches and try to explain one of the pathways in these heterogenous group of patients.

References:

$p = 0.005$; $\text{Ham-D: } 8 \pm 4.5 \text{ Vs. } 12.3 \pm 6.8, p = 0.009$; $\text{CGI-E: } 2.4 \pm 1.3 \text{ Vs. } 3.5 \pm 1.5, p = 0.008$-Man-Whitney U

Conclusions: A little percentage of schizophrenics' relatives received psychoeducational information. However this had a high impact in schizophrenic symptomatology.

References:

NR436  Tuesday, May 4, 3:00 p.m.-5:00 p.m.
Lack of EPS Predicts QOL in Schizophrenics Treated With Clozapine or Atypicals
Sergio A. Streijilevich, M.D., Salud Mental, Area Investigation, Congreso 2477 D, Buenos Aires 1428, Argentina; Ana Palatnik, M.D., Julian Bustin, M.D.; Julieta Cassone, M.D.; Mariana Gimenez, M.D., Soledad Figueroa, M.D., Gabriel de Erausquin, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to compare the QOL in two groups of schizophrenic outpatients under naturalistic conditions of treatment with typical antipsychotics or clozapine.

Summary:
Objectives: To compare the severity of symptoms and quality of life in two groups of schizophrenic outpatients, under naturalistic conditions: (1) non-resistant treated with typical antipsychotics and (2) resistant treated with clozapine.

Hypothesis: Despite their initial greater severity, patients treated with clozapine will have a better quality of life due to a lesser incidence of extrapyramidal symptoms (EPS).

Methods: Two groups of 20 patients each, stable for more than one year and randomly selected were assessed in a cross-sectional basis with the following scales: PANSS, Ham-D, Simpson & Angus, Barnes, AIMS, and QLS. A relative of each patient also completed a self-administered questionnaire evaluating the patient’s quality of life. Non-parametric methods were used for statistical analysis.

Results: No significant differences were found between both groups of patients regarding severity of psychopathology or quality of life, whether assessed by the patients, family members, or clinical evaluators. Patients treated with clozapine had significantly less EPS but more general side effects.

Conclusions: Resistant schizophrenic patients treated with clozapine improve up to the same level than non-resistant patients treated with typical antipsychotics. Resistance to treatment with typical antipsychotics could be given by a greater vulnerability to extrapyramidal effects caused by these medications. The schizophrenic deficit acts as a common ceiling of improvement for both groups.

References:

NR437  Tuesday, May 4, 3:00 p.m.-5:00 p.m.
Neurocognitive Differences Between Patients With Schizophrenia and Patients With Bipolar Disorder With Psychotic Symptoms
Sergio A. Streijilevich, M.D., Salud Mental, Area Investigation, Congreso 2477 D, Buenos Aires 1428, Argentina; Eduardo A. Leiderman, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize some of the neurocognitive differences between schizophrenics and bipolar patients with severe psychotic symptoms.

Summary:
Objective: To investigate the cognitive profiles of schizophrenic and bipolar outpatients that were previously misdiagnosed as schizophrenics due to their severe psychotic symptoms.

Methods: Ten bipolar patients that had on their last episode a score greater than 22 on the PANSS positive and had been previously misdiagnosed as schizophrenics, were compared with 10 schizophrenic patients and 10 controls. Both groups of patients were stabilized for more than six months. Bipolar patients were not medicated with antipsychotics. They were assessed with the WCST and a visual working memory paradigm. Quality of life was assessed.

Results: There were no significant differences between both groups of patients in the visual working memory paradigm but their performance was worse than controls. Bipolar patients made a significant lower number of perseverative errors and a higher number of categories in the WCST than schizophrenics. WCST results correlated with occupational function assessed by QLS.

Conclusions: Bipolar patients with psychotic symptoms have less executive deficits than schizophrenics but similar visual working memory deficits.

References:

NR438  Tuesday, May 4, 3:00 p.m.-5:00 p.m.
What Does Not Improve With Clozapine in Schizophrenia?
Sergio A. Streijilevich, M.D., Salud Mental, Area Investigation, Congreso 2477 D, Buenos Aires 1428, Argentina; Sergio D. Apfelbaum, M.D., Eduardo A. Leiderman, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize which clinical parameters improve after many years of clozapine treatment.

Summary:
Objective: To elucidate which parameters do not improve in schizophrenic patients treated with clozapine.

Methods: We carried out a continuous six year prospective follow up of schizophrenic patients treated with clozapine after being changed from neuroleptic treatment. Assessments at four and 12 weeks, six and 12 months, and six years of clozapine treatment were performed. PANSS, SANS, HAM-D, UPDRS, QLS (Heinrich et al.) scales and Wisconsin Card Sorting Test were
used. Data were analyzed with Repeated Measures Anova and post-hoc Wilcoxon Tests.

Results: Ten patients completed the follow-up. Positive, negative, depressive and extrapiramidal symptoms improved significantly (p<0.001) between weeks 4 and 12 without later changes. All these parameters correlated significantly between them. WCST variables did not change significantly during the six years of treatment. Abstract thought and alogia improved slowly and less significantly (p<0.05).

Conclusions: Negative, depressive, and extrapiramidal symptoms overlap between them and tend to improve simultaneously. Primary deficit is better represented by the WCST because it does not improve and justifies the persistent social and working deficiencies of schizophrenic patients.

References:

NR440 Tuesday, May 4, 3:00 p.m.-5:00 p.m.
Dose-Response Efficacy of Mixed Amphetamine Salts Extended Release in Adults With ADHD Supported by Shire Pharmaceutical Development, Inc.
Stephen V. Faraone, Ph.D., Department of Psychiatry, Massachusetts General Hospital, 15 Parkway Street, Boston, MA 02114; Joseph Biederman, M.D., Thomas J. Spencer, M.D., Timothy E. Wilens, M.D., Richard H. Weisler, M.D., Yuxin Zhang, Ph.D., Simon J. Tulloch, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to: (1) understand the advantages and limitations of real-time monitoring in natural environments using electronic (PDA) diaries; and (2) identify differences between children with ADHD receiving pharmacotherapy and comparison children in behaviors, moods, and quality of family life.

Summary:
Objective: To analyze dose-response relationships for efficacy and safety variables in a six-week, randomized, double-blind, forced-dose escalation study of once-daily mixed amphetamine salts (MAS) XR 20, 40, and 60 mg compared with placebo in adults (aged 18 to 75 y) with ADHD combined type.

Methods: Analysis of covariance was used to test for a dose-response relationship between ADHD-RS scores (primary efficacy) and that does (last observation carried forward), adjusted for time on final dose and baseline severity. Outlier analyses of safety measures, including adverse event (AE) reports, vital signs, and ECGs, were also completed.

Results: We found no significant interaction between MAS XR dose and baseline ADHD-RS score (F(2,45)=5.92, P=0.098). There was a statistically significant dose-response effect (F(5,81)=6.88, P=0.0013) with significant separation between the 40- and 60-mg dose groups (F(1,16)=2.36, P=0.0026). For patients receiving their final MAS XR dose for at least two weeks, the adjusted ADHD-RS change scores were -12.4, -13.0, and -18.6 unit points for the 20-, 40-, and 60-mg groups, respectively. The CGI side effects index indicated fewer side effects relative to therapeutic improvement in the higher dose groups (X2(6)=21.1. P=0.002).

Conclusion: These results indicate a robust dose-response relationship between ADHD symptom reduction and 20-40-, and 60-mg doses of MAS XR in adults with ADHD, but no dose-response relationship for any safety measures.

Funding Source(s): Supported by Shire Pharmaceutical Development Inc.

References:

Funding Source(s): Eli Lilly and Company.

References:
with attention-deficit/hyperactivity disorder. Arch Gen Psych 2001; 58:775–782.

**NR441** Tuesday, May 4, 3:00 p.m.-5:00 p.m.

Prevalence of Adult ADHD in the U.S.
Supported by Shire Pharmaceutical Development, Inc.
Stephen V. Faroone, Ph.D., Department of Psychiatry, Massachusetts General Hospital, 15 Parkway Street, Boston, MA 02114; Joseph Biederman, M.D.

**Educational Objectives:**

After reviewing this poster, the participant should be able to describe the prevalence of ADHD in adults and appreciate the number of adults displaying significant ADHD symptoms.

**Summary:**

**Objective:** To gauge the prevalence of diagnosed attention deficit/hyperactivity disorder (ADHD) and ADHD symptoms in U.S. adults.

**Method:** A telephone survey conducted by RoperASW obtained a weighted sample reflecting the general U.S. population. All subjects were asked if a doctor or mental health professional had diagnosed them with ADHD. Additionally, an 18-question, DSM-IV-based symptom survey was used and subjects were asked to evaluate each symptom retrospectively (as a child in grade school) as well as currently (in the past six months).

**Results:** A weighted sample of 1,000 adults was obtained for analysis. Survey results reveal 4.3% of adults in the U.S. have been diagnosed with ADHD by a health care professional. Forty-three percent were diagnosed by the age of 10 years. However, 35% were not diagnosed until adulthood (at or after the age of 18 years), and 20% were not diagnosed before the age of 30 years. Symptom scores reveal 3% of U.S. adults experienced six or more symptoms of ADHD “often” during childhood and continue to experience these symptoms “often” in adulthood.

**Conclusion:** Based on this survey, 3% of U.S. adults satisfy DSM-IV criteria for the diagnosis of ADHD. Of those adults who have been clinically diagnosed, more than one third were not diagnosed until adulthood.

**Funding Source(s):** Supported by Shire US Inc.

**References:**


**NR442** Tuesday, May 4, 3:00 p.m.-5:00 p.m.

Atomoxetine Treatment in Children With ADHD and Comorbid Tic Disorders
Supported by Eli Lilly and Company


**Educational Objectives:**

At the conclusion of this presentation, the attendee should be aware of the relative risks of current stimulant and nonstimulant treatments for ADHD and that nonstimulant treatments appear to have little or no deleterious effect on tic severity.

**Summary:**

**Objective:** To determine whether atomoxetine exacerbates tics in children with Attention-Deficit/Hyperactivity Disorder (ADHD) and comorbid tic disorders.

**Methods:** Study subjects were patients, 7–17 years old, who met DSM-IV criteria for ADHD and had concurrent Tourette syndrome and/or chronic motor tic disorder.

**Results:** Double-blind atomoxetine treatment (0.5–1.5 mg/kg/day, n=76, up to 18 weeks) was associated with greater reduction of tic severity relative to placebo (n=72), approaching significance on the Yale Global Tic Severity Scale and Tic Severity Self-Report total scores and achieving significance on the Clinical Global Impressions (CGI) tic/neurological severity scale. Atomoxetine patients also showed significantly greater improvement on the Attention-Deficit/Hyperactivity Disorder Rating Scale total score and CGI severity of ADHD/psychiatric symptoms scale. Atomoxetine patients had greater increases in heart rate and decreases of body weight, and rates of treatment-emergent decreased appetite and nausea were significantly higher. No other clinically relevant differences were seen in any other vital sign, adverse event, or electrocardiographic or laboratory parameter.

**Conclusion:** Rather than exacerbating tic symptoms, atomoxetine appeared to decrease severity of reported tics while reducing symptoms of ADHD. Treatment appeared to be safe and well tolerated.

**Funding Source(s):** Funding provided by Eli Lilly and Company

**References:**


**NR443** Tuesday, May 4, 3:00 p.m.-5:00 p.m.

The Costs Associated With ADHD in Adults
Supported by Eli Lilly and Company

Maureen Lage, Ph.D., Outcomes Reasearch, Health Metrics, Route 1, Stonington, CT 06378; Kristina Secnik, Ph.D., Andrine R. Swensen, Ph.D.

**Educational Objectives:**

At the conclusion of this session, the participant should be able to describe the direct and indirect costs associated with adult ADHD.

**Summary:**

**Introduction:** A cohort of adults with attention-deficit/hyperactivity disorder (ADHD) was examined to find the prevalence of comorbidities, the direct medical costs, and the indirect costs of missed work.

**Methods:** A case-control analysis of the direct medical costs and comorbidities of adults with ADHD was conducted from a claims database that was linked to a productivity management database. Inclusion criteria for 2,292 patients consisted of aged 18 years old, diagnosed with ADHD, and had continuous health insurance coverage. These patients were matched with a non-ADHD cohort. Workdays lost were found from a subset of patients.

**Results:** Adults with ADHD were significantly more likely (p<.01) to have a diagnosis of asthma, anxiety, bipolar disorder, depression, drug or alcohol abuse, antisocial disorder, or oppositional
Disorder compared with the control group. Controlling for the impact of comorbidities, adults with ADHD had significantly higher (p<.01) medical costs compared with the non-ADHD cohort. Employees diagnosed with ADHD were significantly (p<.01) more likely to be absent from work.

**Conclusion:** Adults with ADHD were found to incur more medical direct costs from the provision of health care services than a cohort of non-ADHD patients. They have a higher rate of absenteeism and reported more comorbidities.

**Funding Source(s):** Funding provided by Eli Lilly and Company

**References:**

**NR444**

**Tuesday, May 4, 3:00 p.m.-5:00 p.m.**

**Dose and Time Response of Atomoxetine Use in Adult ADHD**

**Supported by Eli Lilly and Company**

Lenard A. Adler, M.D., Department of Psychiatry, New York University School of Medicine, 530 First Avenue HCC 5A, New York, NY 10016-6497; Thomas J. Spencer, M.D., Virginia Sutton, Ph.D., Calvin R. Summer, M.D.

**Educational Objectives:**
At the conclusion of this session, the participant should be able to: (1) understand how weight-based dosing may affect adult ADHD symptom improvement; (2) determine if time course of treatment affects adult ADHD symptom improvement.

**Summary:**
**Objective:** To determine if a patient's dose (weight-based and total) or treatment duration affects the extent of treatment response to atomoxetine.

**Methods:** Adult patients (N=384) were given open-label treatment with atomoxetine (maximum dose 160mg/day). After up to 10 weeks of treatment, and again after up to 97 weeks of treatment, response was evaluated using the Conners' Adult ADHD Rating Scale: Investigator (CAARS:lnv) Total ADHD Symptom score and the Clinical Global Impression-Severity (CGI-S) score to examine possible effects of dose (weight-based and total) and duration of treatment.

**Results:** Significant symptom improvement was noted acutely and maintained throughout the duration of treatment. There was a significant dose response on the CAARS:lnv when patients were classified by their weight-based dose after up to 97 weeks of treatment. The pattern of response was similar to that seen in the atomoxetine arm of a previous pediatric dose-response study. In addition, patients taking higher total doses or higher weight-based doses were more likely to show a clinical response to atomoxetine.

**Conclusions:** Greater symptom improvement was seen in the higher dose groups. The pattern of increased response with increased dose was similar, whether patients were classified according to weight-based or total daily dose.

**Funding Source(s):** Funding provided by Eli Lilly and Company

**References:**

**NR445**

**Tuesday, May 4, 3:00 p.m.-5:00 p.m.**

**Quality-of-Life Assessment in Atomoxetine-Treated Adult ADHD Patients**

**Supported by Eli Lilly and Company**

Lenard A. Adler, M.D., Department of Psychiatry, New York University School of Medicine, 530 First Avenue HCC 5A, New York, NY 10016-6497; Douglas K. Kelsey, M.D.; Anthony P. Dietrich, M.D.; Frederick W. Reimherr, M.D.; Bart R. Sangal, M.D.; Keith Saylor, Ph.D.; Kristina Secnik, Ph.D.; Virginia Sutton, Ph.D.; Rodney J. Moore, Ph.D.

**Educational Objectives:**
At the conclusion of this session, the participant should be able to: (1) understand how weight-based dosing may affect adult ADHD and how those problems relate to ADHD symptoms; (2) understand how treatment of adults with ADHD may improve both symptom quality and life.

**Summary:**
**Objective:** To determine if atomoxetine treatment improves adult ADHD symptoms and measures of overall mental health.

**Methods:** ADHD patients (ages 18–50) were diagnosed using standardized, semi-structured interviews. Exclusion criteria included comorbid anxiety and mood disorders. 172 patients who met entry criteria were treated with atomoxetine (80 mg/day). Patients completed the Medical Outcomes Study 36-Item Short-Form Health Survey, four-week recall (SF-36) and investigators rated ADHD (Conners’ ADHD Rating Scale-Investigator Rated: Screening Version (CAARS-lnv:SV) at baseline and after six weeks of treatment. Mean change from baseline to endpoint was analyzed via Wilcoxon signed-rank test.

**Results:** Baseline SF-36 normative scores for scales reflecting physical health were all above 50 and improved only modestly (Gain: +1.5±0.64, p<.002, General Health: +1.19±0.45, p<.001; Physical Functioning: +0.21±0.52, p=.198; Role Physical: −0.08±0.74, p=.992). Baseline scores on scales reflecting mental health were below 50, all improving significantly at endpoint (Role Emotional: +3.37±0.94, p<.001, Mental Health: +4.21±0.68, p<.001, Social Function: +3.19±0.83, p<.001, Vitality: +2.83±0.64, p<.001). ADHD symptoms also improved (CAARS-lnv:SV ADHD Total Score: baseline=37.80, mean change=−15.34±0.77, p<.001); this change correlates with changes in mental health.

**Conclusions:** Untreated adult ADHD patients are below average on measures of overall mental health. Atomoxetine significantly improves functioning in these areas and in ADHD symptoms.

**Funding Source(s):** Funding provided by Eli Lilly and Company

**References:**
NR447  Tuesday, May 4, 3:00 p.m.-5:00 p.m.
Self-Report Rating Scale for Psychiatric Symptoms in Adults With ADHD
Kenneth D. Gadow, Ph.D., Psychiatry Department, State University of New York, Putnam Hall, Stony Brook, NY 11794-8790; Margaret D. Weiss, M.D., Joyce Sprafkin, Ph.D.

Educational Objectives:
At the conclusion of this session, participants should be able to describe the psychometric properties of the ASRI-4 and indicate how the ASRI-4 could facilitate diagnostic evaluations.

Summary:
Objective: Few rating scales of adult ADHD assess comorbid symptoms. This study evaluates the reliability and validity of the Adult Self-Report Inventory-4 (ASRI-4), a norm-referenced ratings scale of DSM-IV psychiatric symptoms.

NR448  Tuesday, May 4, 3:00 p.m.-5:00 p.m.
Parental Assessment of Personality Changes While on Stimulants Versus Atomoxetine
Supported by Eli Lilly and Company
Rakesh Jain, M.D., Psychopharmacology Department, Research and Development, Clinical Research, 135 Oyster Creek Drive, Suite G, Lake Jackson, TX 77566-4118; Saundra Jain, M.A.

Educational Objectives:
At the conclusion of this session, the participant should better understand the adverse personality effects of stimulants vs. atomoxetine in children and adolescents.

Summary:
Introduction: Parents' perceptions of personality changes caused by stimulant treatment of ADHD are a frequent complaint in clinical practice. Anecdotally, atomoxetine, a new treatment option for ADHD, is reported by parents to have fewer negative adverse effects on their children's personalities. This study is more systematically capture parents' perceptions on this issue.

Method: This is a retrospective analysis of 20 children and adolescents with ADHD. ADHD kid's parent's perceptions that, in the past, experienced mood and personality difficulties on stimulants, who because of these issues were switched to atomoxetine.

Results: Impairment was assessed on a 0–5 scale (none, mild, moderate, severe and very severe impairment). On the question "Did the medication have a negative effect on personality", the mean for stimulant response was 2.95 vs. 0.15 for atomoxetine (p<.0001). Q: "Does the medication make the child more cranky or irritible" the means response for stimulant exposure was 2.50 vs 0.20 for atomoxetine (p=0.0009). Q: "Did the child lose sparkle in personality", the results are stimulant mean 2.95 vs. 0.10 for atomoxetine (p=0.0005). On another question "Did the child act like a zombie" stimulant mean was 1.5 vs 0.0 for atomoxetine (p=0.002). There are other personality dimensions evaluated.

Conclusions: Based on parents' perceptions, should treatment with stimulants cause personality changes, a switch to atomoxetine appears to be an acceptable alternative.

Funding Source(s): Eli Lilly & Company
NR449  Tuesday, May 4, 3:00 p.m.-5:00 p.m.
Retrospective Chart Review of Neuropsychological Tests of Frontal Lobe Function and Aggression in ADHD
Paula Gaudino, M.S.W., Neuropsychiatry Department, Riverside Hospital, 4460 MacArthur Boulevard, N.W., Washington, DC 20007; Mark J. Smith, M.D., Sidney Binks, Ph.D.

Educational Objectives:
At the conclusion of this session, participants should know the relationship between various neuropsychological indices of frontal functioning and aggression in adolescents.

Summary:
Objective: Frontal function is important in controlling aggression in children and adolescents with attention deficit hyperactivity disorder (ADHD). Few studies have simultaneously examined many different aspects of frontal function. This study tests the effect of five different indices of frontal function on aggression in children and adolescents with ADHD.

Method: We retrospectively examined 78 charts of ADHD children and adolescents given the Woodcock Johnson III: Test of Cognition (WJ-III), Continuous Performance Test (CPT) and Buss Perry Aggression Questionnaire (New-Buss Version). A one-way ANOVA using five measures of frontal function, i.e., Concept formation, Numbers Reversed, and Visual-Auditory Learning from the WJ-III, along with Omission Errors and Commission Errors from the CPT as independent variables and scores of the Buss Perry Aggression Questionnaire as dependent variable was used.

Results: There is a statistically significant difference between mean scores of the CPT scores and aggression levels. Higher scores of CPT commission errors predicted higher levels of aggression. There were no other significant differences.

Conclusion: Commission errors on the CPT are considered a measure of impulsivity. It appears from these results that control of impulsivity is an important frontal function in determining levels of aggression in ADHD children and adolescents.

References:

NR450  Tuesday, May 4, 3:00 p.m.-5:00 p.m.
Analog Classroom Study of Amphetamine Extended Release and Atomoxetine in Youth With ADHD
Supported by Shire Pharmaceutical Development, Inc.
Sharon Wigal, Ph.D., Pediatrics Department, University of California, Irvine, 19722 MacArthur Boulevard, Irvine, CA 92697-4486; James J. McCough, M.D., Kelly Posner, Ph.D., Scott H. Kollins, Ph.D., M. Alex Michaels, M.D., Simon J. Tulloch, M.D.

Educational Objectives:
At the conclusion of this session, the participant should better understand the treatment outcomes with OROS® MPH and atomoxetine in children with ADHD.

Summary:
Objective: Compare core symptom improvement of OROS® MPH and atomoxetine in children with attention-deficit/hyperactivity disorder (ADHD).

Methods: Prospective, randomized (2:1), open-label, three-week study of OROS® MPH and atomoxetine in ADHD children.
16-mile road course. Driving competency was assessed by a rater blinded to the medication condition.

Results: Impulsive driving errors occurred rarely, under both medication and no medication conditions. The mean number of inattentive driving errors was significantly higher off medication compared to on medication (7.8 vs. 4.6/driver, p<.01). The improvement in driving performance (change in the number of inattentive errors) was positively correlated with medication dosage (r=6.0, p=.01).

Conclusion: Once-daily OROS® MPH improves actual driving performance of adolescent males diagnosed with ADHD. In particular, driving errors arising from inattention are significantly reduced.

This study was supported by McNeil Consumer & Specialty Pharmaceuticals, Fort Washington, PA.

References:

NR453
Tuesday, May 4, 3:00 p.m.–5:00 p.m.
Patient-Recorded Electronic Diaries Assessing Adherence in ADHD Adolescents
Supported by McNeil Pharmaceuticals
James J. McGough, M.D., UCLA Neuropsychiatry Institute, 300 UCLA Medical Plaza, Los Angeles, CA 90095; Suzanne Lamerand, B.S.

Educational Objectives:
At the conclusion of this session, the participant should be able to: (1) understand different means of assessing patient adherence to pharmacotherapeutic regimens; (2) understand that patient-recorded electronic diaries may be a useful means of assessing adherence to medication.

Summary:
Objective: To assess the accuracy of patient-recorded electronic diaries for determining medication adherence to once-daily OROS® methylphenidate (MPH) in adolescents with attention-deficit/hyperactivity disorder (ADHD). Patient adherence to pharmacotherapeutic regimens is important to ensure that efficacy is achieved. However, currently available methods for assessing adherence are often cumbersome. Patient-recorded electronic diaries may permit consistent but more efficient assessment of treatment adherence.

Methods: During a 2-week double-blind study phase, 177 ADHD adolescents (13–18 years) were randomized to receive individually determined doses of once-daily OROS® MPH (18, 36, 54, or 72 mg) or placebo. At baseline visit, subjects were given a Handspring™ Visor Handheld PDA with eCaseLink™ e-Patient diary software and were instructed to enter the following information daily: date, time of taking dose, number of tablets taken. Unused tablets were returned at the next study visit and subjects received the correct number of tablets for the following week.

Results: According to tablet counts, 92% (OROS® MPH) and 94% (placebo) of subjects were ≥80% adherent. Similarly, data from the electronic diaries indicated that 94% (OROS® MPH) and 97% (placebo) of subjects were ≥80% adherent. There was also good agreement between the two methods for data from individual subjects: correlation between methods 89% (OROS® MPH), 87% (placebo).
Conclusions: This study in ADHD adolescents suggests patient-recorded electronic diaries may provide a valuable means of assessing subject medication adherence during clinical studies. Study supported by McNeil Consumer & Specialty Pharmaceuticals, Fort Washington, PA.

References:

NR454 Tuesday, May 4, 3:00 p.m.–5:00 p.m.
Effects of Long-Term Atomoxetine Treatment for Young Children With ADHD
Supported by Eli Lilly and Company
Christopher J. Kratochvil, M.D., Psychopharmacology Research Center, University of Nebraska Medical Center, 985581 Nebraska Medical Center, Omaha, NE 68198-5561; Timothy E. Wilens, M.D., Laurence L. Greenhill, M.D., Hailiao Gao, Ph.D., Christine Thomason, Ph.D., Douglas L. Gelowitz, Ph.D.

Educational Objectives:
At the conclusion of this session the clinician will have an understanding of the long-term tolerability and efficacy of atomoxetine in young children with ADHD.

Summary:
Objective: To date, few clinical investigations of attention-deficit/hyperactivity disorder (ADHD) extend beyond a few months. The purpose of this presentation is to report on the efficacy and tolerability of atomoxetine treatment among young children with ADHD.

Method: Data from 6- and 7-year-old children (n=192) enrolled in similarly designed clinical trials that met the DSM-IV criteria for ADHD were pooled. The children had a minimum of 12 months of atomoxetine treatment and 95 (49%) received treatment for up to 24 months. The mean modal dose (±SD) of atomoxetine was 1.55 mg/kg/day (0.32). The primary efficacy outcome measure was the mean change from baseline to endpoint in the ADHD Rating Scale -IV (ADHD RS). The Conners’ Parent Rating Scale-Revised: Short Form (CPRS-R:S) was a secondary efficacy measure.

Results: The effectiveness of atomoxetine treatment for children was maintained over a 12 to 24 month period as demonstrated by ADHD RS total and T-scores. Adverse events were clinically minor and transient, and only 1.6% of children discontinued due to adverse events. There were no clinically meaningful changes in lab tests.

Conclusion: Long-term atomoxetine treatment appears to be well-tolerated and effective in young children with ADHD.

References:

NR455 Tuesday, May 4, 3:00 p.m.–5:00 p.m.
Efficacy of Dexmethylphenidate Extended Release Capsules in Adults With ADHD
Supported by Novartis Pharmaceuticals Corporation
Thomas J. Spencer, M.D., Department of Psychiatry, Massachusetts General Hospital, 55 Fruit Street, Warren 705, Boston, MA 02114; Sam Kim, H. Jiang

Educational Objectives:
At the conclusion of this session, the participant should be able to discuss the efficacy of once-daily dexmethylphenidate extended-release (d-MPH-ER) capsules compared with placebo in adults with attention-deficit/hyperactivity disorder (ADHD).

Summary:
Objective: To evaluate the efficacy of once-daily dexmethylphenidate extended-release (d-MPH-ER) capsules compared with placebo in adults with attention-deficit/hyperactivity disorder (ADHD). Dexmethylphenidate is the pharmacologically active d-threo enantiomer of MPH.

Method: This was a multicenter, double-blind, parallel-group, placebo-controlled study. Two hundred twenty-one adults diagnosed with ADHD according to DSM-IV criteria were randomized; 184 completed the double-blind phase. Patients were randomized to one of four treatments: d-MPH-ER 20 mg, 30 mg, 40 mg, or placebo once daily for five weeks. Efficacy was evaluated using DSM-IV ADHD Rating Scale total scores.

Results: At final visit, mean change from baseline 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 (all P values vs placebo). The proportion of patients with ≥30% improvement at final visit was 34.0% for placebo, 57.9% for d-MPH-ER 20 mg (P=.017), 53.7% for d-MPH-ER 30 mg (P=.054), and 61.1% for d-MPH-ER 40 mg (P=.007). Safety and tolerability were consistent with those of immediate-release d-MPH and MPH.

Conclusion: In once-daily doses of 20 mg, 30 mg, or 40 mg, d-MPH-ER is a safe, effective treatment for adult patients with ADHD. This study was supported by Novartis Pharmaceutical Corporation.

References:

NR456 Tuesday, May 4, 3:00 p.m.–5:00 p.m.
Safety and Efficacy of Mixed Amphetamine Salts Extended Release in Children With Oppositional Defiant Disorder (ODD)
Supported by Shire Pharmaceutical Development, Inc.
Thomas J. Spencer, M.D., Department of Psychiatry, Mass General Hospital, 55 Fruit Street, Warren 705, Boston, MA 02114; Joseph Biederman, M.D., Howard Abikoff, Ph.D., Steven R. Pliszka, M.D., Samuel Boellner, Frank A. Lopez, M.D., Simon J. Tulloch, M.D.

Educational Objectives:
After reviewing this poster, the participant should be able to discuss the safety and efficacy of mixed amphetamine salts extended release (MAS XR) for the treatment of oppositional defiant disorder (ODD) in children ages 6 to 17.
Summary:

Objective: To assess the safety and efficacy of mixed amphetamine salts extended release (MAS XR) 10, 20, 30, or 40 mg once daily compared with placebo for the treatment of oppositional defiant disorder (ODD) in children and adolescents (aged 6 to 17 years).

Methods: A randomized, double-blind, multicenter, parallel-group, forced-dose-escalation study of 308 participants who met DSM-IV-TR criteria for ODD (with or without comorbid ADHD). Primary efficacy was assessed at baseline and weekly for four weeks using a 10-item revised SNAP-IV (Swanson, Nolan, Pelham) Parent Rating Scale for ODD. Safety and tolerability were assessed by spontaneously reported adverse events (AEs), vital signs, ECGs, and laboratory measures.

Results: The ITT population included 297 children (mean age 10.6 y) with ODD; 79.1% (235) had comorbid ADHD and 20.9% (62) had ODD simplex. At endpoint, MAS XR significantly reduced ODD symptoms compared with placebo (ANCOVA, P = 0.025). The 30-mg MAS XR treatment group had the largest reduction in ODD symptoms, with a least square mean difference from placebo of −0.43 unit points on the SNAP-IV ODD scale (95% CI −0.74 to −0.11, P = 0.0043). The most commonly reported treatment-emergent AEs were anorexia (25.3%), insomnia (19.5%), headache (18.5%), and abdominal pain (10.7%). Only 14 patients withdrew from the study because of AEs.

Conclusion: MAS XR is effective for treating ODD in children and adolescents. Higher doses appear to be more effective in patients with ODD and comorbid ADHD. Overall, treatment was well tolerated.

Supported by Shire Pharmaceutical Development Inc.

References:


NR457 Tuesday, May 4, 3:00 p.m.-5:00 p.m.

Ziprasidone’s Brightening Effect in Mental Retardation: Cases

Supported by Pfizer Inc.

Seth A. Cohen, M.D., 150 Nickerson Street, Suite 108, Seattle, WA 98109

Educational Objectives:

At the conclusion of this presentation, the participant should understand the potential novel benefits of atypical antipsychotic therapy in patients with mental retardation and behavioral disturbances.

Summary:

Objective: To evaluate ziprasidone’s effects on mood and behavior in mentally retarded inpatients with histories of assault self-injury, or property destruction.

Methods: This retrospective chart review comprised 82 mentally retarded adults given ziprasidone because of maladaptive behaviors or significant metabolic disturbances (≥7% weight gain, increased lipid or glucose levels) associated with other atypical antipsychotics.

Results: Age range was 17–68 years. 48 (58.5%) patients had severe-to-profound deficits, and 33 (40.2%) had concomitant seizure disorders. Duration of ziprasidone therapy was 1–32 months (mean 18.6 months); total daily dosing was 20–280 mg (mean 104.6 mg). Besides improving maladaptive and compulsive behaviors, as well as metabolic parameters, ziprasidone induced a “brightening” of mood and affect in 29 (35.4%) of patients. Brightening was expressed as greater social engagement, expressiveness, and friendly demeanor. Some patients (n=14) whose behaviors improved experienced agitation, which generally responded to dosage increases or beta-blockade. Three patients given ziprasidone for ≥29 months will be described in detail.

Conclusion: Ziprasidone safely controls maladaptive behaviors in mentally retarded adults and, importantly, improves mood and social engagement. “Brightening” may reflect improvements in primary presenting symptoms, an effect on prosocial behaviors, or a mild antidepressant effect from serotonin and norepinephrine reuptake inhibition.

Funding Source(s): Pfizer Inc.

References:

1. Harvey PD, Loebelel A, Siu CO, Romano SJ, Murray S. Cogni-
vive, affective, prosocial improvement after switch to zipra-
sidone. Presented at the 55th Institute on Psychiatric Services
of the American Psychiatric Association; October 29–Novem-
ber 2, 2003; Boston, MA, USA.


NR458 Tuesday, May 4, 3:00 p.m.-5:00 p.m.

PTSD Linked to Sex Risks in Women Veterans With Depression

Marian I. Butterfield, M.D., Department of Psychiatry, Durham VA Medical Center, 508 Fulton Street, Box 152, Durham, NC 27705; Jennifer L. Strauss, Ph.D., Karen M. Stieuchak, M.S., Christine E. Marx, M.D., Jeffrey W. Swanson, Ph.D., Marvin S. Swartz, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to: (1) recognize the relationship between lifetime sexual trauma and PTSD among women veterans; and (2) discuss the links between PTSD and high sex-risk behaviors in women with depression.

Summary:

Objective: PTSD is associated with high rates of sexual risk behaviors in incarcerated women. We hypothesized that comorbid PTSD is linked to risk behaviors in women veterans with depression, and that sexual trauma would account for this association.

Methods: Outpatient women veterans (N = 150) with depression were assessed for comorbid PTSD using the PTSD Checklist (PCL) and lifetime sexual trauma and risk behaviors. Bivariate and logistic regression analyses were conducted.

Results: Mean age was 46, 52% were Caucasian, 36% were married, 63% had PTSD. Women with PTSD did not differ on age, race, childhood sexual trauma, or current substance abuse, but were more likely to report adult forced sex (65.3% vs 45.5% p = 0.03) and less likely to be married (29.5% vs 47.3% p = 0.03). Those with PTSD were more likely to report unprotected sex for money/gifts or drugs (OR = 3.29; 95% CI = 1.17 – 9.23). Tests of mediation indicated that adult forced sex partially accounted for this association and that women who reported adult forced sex were more likely to report sex risk behaviors (OR 3.46; 95% CI = 1.21 – 9.86).

Conclusion: Findings suggest that PTSD conveys increased risk of lifetime sexual-risk behaviors in this cohort and is partially mediated by history of adult forced sex. Given high rates of military
sexual trauma and PTSD, assessment of sex-risk behaviors in women veterans is warranted.

**Funding Source(s):** This research was funded by the Department of Veterans Affairs through a research career development award to the first author (RCD-0019-2) and the VA Cooperative Studies Program (CSP706D).

**References:**


**NR459**

**Tuesday, May 4, 3:00 p.m.-5:00 p.m.**

**Comorbid PTSD is Associated With Increased Suicidality and DHEA in Women**

Marian I. Butterfield, M.D., Department of Psychiatry, Durham VA Medical Center, 508 Fulton Street, Box 152, Durham, NC 27705; William T. Trost, Jennifer L. Strauss, Ph.D., Karen M. Stechuchak, M.S., Kathryn M. Connor, M.D., Courtney Mackuen, Jonathan R.T. Davidson, M.D., Christine E. Marx, M.D.

**Educational Objectives:**

At the conclusion of this session, the participant should be able to: (1) define neurosteroids and discuss potential alterations in PTSD; and (2) discuss potential relationships between neurosteroids and co-morbid PTSD in women with depression.

**Summary:**

**Objective:** High rates of suicidality in male veterans with PTSD are linked to the neurosteroid DHEA. Thus, we evaluated if comorbid PTSD is associated with suicidality and DHEA alterations in women veterans with depression.

**Methods:** Treatment seeking women veterans (n=158) with depression were assessed using a risk interview and the PTSD check list (PCL). Serum from morning blood draws was used to determine neurosteroid levels across one biosynthetic pathway (dehydroepiandrosterone (DHEA) → androstenedione → testosterone → estradiol) using standard radioimmunoassays. Bivariate (chi-square or t-test as appropriate) and logistic regression analyses were conducted.

**Results:** Mean age was 45; 42.4% were African American, 35.4% were married. Over half met DSM-IV criteria for PTSD (65%, n = 103). Women with PTSD did not differ from those without PTSD with respect to age, race or marital status, but were more likely to have been raped (62.1% vs 43.6% p = 0.03). Women with PTSD had higher rates of suicidal ideation (44.7% vs 25.5% p = 0.02) and higher mean DHEA levels (8.1 ng/ml vs 5.9 ng/ml p = 0.04) than those with out PTSD. A trend for an association between DHEA levels and suicidality in the PTSD group persisted after controlling for age and time of blood draw (p=0.07).

**Conclusions:** Comorbid PTSD conveys increased risk for suicidal ideation among women veterans with depression. Neurosteroids such as DHEA may be clinically relevant to PTSD and related suicidality. More research is warranted.

**Funding Source:** A VA research career development award to the first (RCD-0019-2) author and the VA Cooperative Studies Program (CSP706D) and NIMH K23 Award to the last author.

**References:**


**NR460**

**Tuesday, May 4, 3:00 p.m.-5:00 p.m.**

**Attachment Representations in ADHD Children Aged Five to Seven Years**

Peter Nagy, M.D., Vadaskert Clinic, Huvosvolgy ut 116, Budapest 1021, Hungary; Luca Farkas, M.A., Julianna Gadoros, M.D.

**Educational Objectives:**

At the conclusion of this session, the participant should be able to see that the child plays an important role in disorganized attachment.

**Summary:**

**Objective:** Several studies point to the fact that ADHD children’s attachment tends to be disorganized. Disorganized attachment is largely attributed to the parenting style, although evidence is accumulating that it might have a genetic background on the part of the child as well. In Hungary, parenting style is largely different from that in the UK or the US (e.g. babysitting is very unusual). With ADHD frequency being about the same as in other countries, we wanted to see whether the different parenting style affects the rate of insecure attachment found among ADHD children.

**Method:** we included 40 5–7-year-old children with a diagnosis of ADHD, who were admitted to a child psychiatry clinic. Mentally retarded children were excluded. Children were administered the Manchester Child Attachment Story Task, and a neuropsychological test battery.

**Results:** Disorganized—attachment rate among ADHD children is very similar to other studies’ results. **Conclusions:** results suggest that noncultural factors play a significant role in disorganized attachment, and although important, parenting style has a smaller influence.

**Funding Source(s):** Hungarian National Fund NKFP-AA/0008/2002

**References:**


**NR461**

**Tuesday, May 4, 3:00 p.m.-5:00 p.m.**

**Brief Parent and Teacher Rating Scale in ADHD Evaluation**

Attila Turgay, M.D., Department of Psychiatry, Scarborough Hospital, 3030 Birchmount Road, Toronto, ON M5G 2C4, Canada; Daniella Mares, Allan McCluckie, M.S.W., Michael Schwartz, Ph.D.

**Educational Objectives:**

At the conclusion of this session, the participant should understand the use of BRIEF Parent and Teacher Rating Scale in the evaluation of ADHD executive functions.
Summary:

Objective: Behavior Rating Inventory of Executive Function (BRIEF) is a parent and teacher questionnaire for studying executive functioning in children and adolescents. This study examined the use of BRIEF in ADHD evaluation of children and adolescents. This study examined differences in comorbid disorders among children and adolescents with ADHD in a large metropolitan teaching hospital. The study sample consisted of 447 males and 147 females (age range: 13-18 years old) with ADHD. BRIEF findings were compared.

Findings: The behavioral index of the BRIEF ("inhibition", "shift" and "emotional control" executive functions) was found to have a significant correlation at 0.1 level with BRIEF ratings (Pearson Correlation .549). The "Inhibition" subscale predicted scores above the 93rd percentile of the DuPaul Hyperactivity/Impulsivity sub-scale symptoms. The "Shift" scores correlated highly with "Inattentive" symptoms. Four subscales of the BRIEF (Initiate, Plan/Organize, Working Memory and Shift (p<.001, p=0.01, p=0.32, p<0.01) were correlated with DuPaul Inattentive Scale scores.

Conclusions: The BRIEF provides reliable information about the executive functions in ADHD. It correlates highly with clinician diagnoses and ADHD symptoms.

References:

NR462 Tuesday, May 4, 3:00 p.m.-5:00 p.m.
Gender Differences in Comorbid Disorders in Adolescents With ADHD
Atilla Turgay, M.D., Department of Psychiatry, Scarborough Hospital, 3030 Birchmount Road, Toronto, ON M5G 2C4, Canada; Joanna Blanchard, M.A., Rubaba Ansari, M.A., David Ng, M.D., Nadeem Chaudhry, M.D., Allan McCluckie, M.S.W., Atique Muhammad, M.D., Canada;

At the conclusion of this session, the participant should be able to recognize the association between dysthymic disorder (DD) and other major psychiatric disorders such as ADHD, conduct disorder, and anxiety disorders.

Summary:

Objective: to study comorbidities of dysthymic disorder in children and adolescents.

Method: Patients were assessed by a child and adolescent psychiatrist using DSM-IV criteria, semi-structured patient and parent interviews, Gadow-Sprafkin Child Symptom Inventory IV, Offord-Boyle Ontario Child Health Checklist and the DuPaul ADHD Rating Scales.

Sample: A total of 240 patients (92 females; 148 males) (age range: 4-18 years) who were diagnosed with DD over the past eight years were assessed.

Findings: The most common comorbid disorders were ADHD (62.91%); oppositional defiant disorder (41.66%), conduct disorder (29.16%), and generalized anxiety disorder (28.33%). ADHD subtypes were: hyperactive-impulsive (0.66%); predominantly inattentive (39.73%) and combined type (59.60%). There were no significant gender differences. It should be noted that this study was conducted in a metropolitan mental health center with a large ADHD clinic; hence, the rate of ADHD in this sample may be higher than the rate seen in the general population.

Conclusions: DD is commonly associated with other psychiatric disorders. The presence of multiple psychiatric disorders in DD may require different medication and/or treatments. Since different medications may be required for different comorbidity profile, the use of general psychopathology rating scales, structured or semi-structured interviews are essential for effective treatment.

References:

NR463 Tuesday, May 4, 3:00 p.m.-5:00 p.m.
Comorbidities of Dysthymic Disorder in Children and Adolescents
Atilla Turgay, M.D., Department of Psychiatry, Scarborough Hospital, 3030 Birchmount Road, Toronto, ON M5G 2C4, Canada; Rubaba Ansari, M.A., Llewelyn W. Joseph, M.D., David Ng, M.D., Aruz Mesci, Michael Schwartz, Ph.D., Joanna Blanchard, M.A.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the association between dysthymic disorder (DD) and other major psychiatric disorders such as ADHD, conduct disorder, and anxiety disorders.

Summary:

Objective: to study comorbidities of dysthymic disorder in children and adolescents.

Method: Patients were assessed by a child and adolescent psychiatrist using DSM-IV criteria, semi-structured patient and parent interviews, Gadow-Sprafkin Child Symptom Inventory IV, Offord-Boyle Ontario Child Health Checklist and the DuPaul ADHD Rating Scales.

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Conclusions: DD is commonly associated with other psychiatric disorders. The presence of multiple psychiatric disorders in DD may require different medication and/or treatments. Since different medications may be required for different comorbidity profile, the use of general psychopathology rating scales, structured or semi-structured interviews are essential for effective treatment.

References:

NR464 Tuesday, May 4, 3:00 p.m.–5:00 p.m.
Gender Differences in ADHD Comorbidity in Children
Atilla Turgay, M.D., Department of Psychiatry, Scarborough Hospital, 3030 Birchmount Road, Toronto, ON M5G 2C4, Canada; Rubaba Ansari, M.A., Aruz Mesci, David Ng, M.D., Llewelyn W. Joseph, M.D., Michael Schwartz, Ph.D., Joanna Blanchard, M.A.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the frequent comorbid disorders and their gender differences associated with ADHD in children and develop specific treatment alternatives.

Summary:
Objective: Most ADHD comorbidity studies are based on small samples and do not provide information on gender differences for comorbidities in specific age groups. This study examined gender differences in comorbidity in 1655 children.
Method: Patients were diagnosed by a child psychiatrist according to DSM-IV criteria, DuPaul ADHD Rating Scale, and Oxford-Boyle Child Health Study (Parent and Teacher) rating scales and Gadow-Sprafkin Child Symptom Inventory 4. The sample consisted of 1318 (79.64%) males and 337 (20.36%) females (6–12 years of age). They were seen in an ADHD clinic of a large teaching hospital.
Findings: Most patients (77.89%) suffered from two or more disorders. Oppositional defiant disorder, conduct disorder, and anxiety disorders were the most common (60.36%, 19.27%, 11.30% respectively). Dysthymic disorder, pervasive developmental disorders, and major depression (4.05%, 3.50%, 2.30% respectively) were also observed. A greater number of males were observed across most comorbidities (ratios ranged from 3.2:1 to 5.6:1). However, females were more likely to have comorbid anxiety disorders or dysthymic disorder than males (13.35% vs. 10.77%, 5.04% vs. 3.79% respectively)
Conclusions: The use of rating scales and/or structured interviews in the assessment of comorbidities is essential, as the treatment/medications chosen may differ according to the specific comorbidity profile.

References:

NR466 Tuesday, May 4, 3:00 p.m.–5:00 p.m.
Frontostriatal Pathology in Neurodevelopmental Disorders
Zsanett Tarnok, M.A., Vadaskert Clinic, Huvosvolgyi Ut 116, Budapest 1021, Hungary; Balazs Aczel, Emese Boglar, M.A., Luca Farkas, M.A., Julianna Gadoros, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize executive function deficits in ADHD and Tourette syndrome.

Summary:
Objective: To evaluate the effect of tic severity on neuropsychological performance in Tourette syndrome (TS).
Method: 48 children with TS diagnosis participated in the study. We used the Yale Global Tic Severity Scale (YGTTSS) to assess the severity of vocal and motor tics. We also used a battery of executive tests which measure cognitive functions such as organization, planning, inhibition, working memory (Wisconsin Card Sorting Test, Stroop Test, Trail Making Test, Digit Span, Word Fluency.)
Results: There was only one correlation with high significance between the severity of vocal tics and the Stroop interference score, which indicates difficulties of inhibiting irrelevant stimuli in TS.
Conclusions: The results suggest that the severity of tics does not influence overall performance in these specific neuropsychological tests, except the increase of interference in conflicting stimuli, which raise the possibility that this function might be a specific feature of TS.
Funding Sources: Hungarian National Fund NKFP-1A/0008/2002.

References:

NR465 Tuesday, May 4, 3:00 p.m.–5:00 p.m.
The Effect of Tic Severity on Executive Functions in Tourette’s Syndrome
Zsanett Tarnok, M.A., Vadaskert Clinic, Huvosvolgyi Ut 116, Budapest 1021, Hungary; Balazs Aczel, Emese Boglar, M.A., Luca Farkas, M.A., Julianna Gadoros, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize inhibition and interference control problems in TS with severe vocal tics.
lar origination and a common neurodevelopmental feature in these disorders.

**Funding Source:** Hungarian National Fund NKFP-1A/0008/2002.

**References:**

2. Brand, Nico; Geenen, Rinie; Oudenhoven, Milo; Lindenborn, Bastiaan; van der Ree, Annette; Cohen-Kettenis, Peggy; Buitelaar, Jan K, Cognitive Functioning in Children With Tourette's Syndrome With and Without Comorbid ADHD. Journal of Pediatric Psychology. 27(2):203–208, March 2002.

**NR467 Tuesday, May 4, 3:00 p.m.–05:00 p.m.**

**Pediatric Psychiatric Emergencies: Who Are They and What Happens to Them?**

Deborah M. Weisbrodt, M.D., Psychiatry Department, Stony Brook University, Putnam Hall, Stony Brook, NY 11794–8790; Gabrielle Carlson, M.D., Jamie S. Hirsch

**Educational Objectives:**

At the conclusion of this session, the participant should learn about the diagnoses and outcome of child and adolescent psychiatric emergencies.

**Summary:**

**Objective:** Changes in access to treatment has led to increased emergency room use in many specialties. In child/adolescent psychiatry, this appears to be true as well. This study examines the reasons for referral to a psychiatric emergency room in 1989, when 128 patients under age 18 were seen for the entire year, and 2001 when 169 youths were seen in the month of March alone.

**Method:** Data from a historic data base were compared with systematically examined youth referrals in one month.

**Results:** There has been a relative increase in children >age 13 (from 21%–30%, p=0.065), and a significant (p<0.000) increase in aggressive behavior (24–52%), male patients (46–64%), brought in by police (17–37%) with resulting decrease in suicidal behavior, substance abuse, and depression being seen as emergencies. Ethnic distribution remained unchanged (78% white, 9% each, black and Hispanic, 4% other). Youth in special education climbed from 24–37%.

**Conclusion:** Aggressive behavior is the major reason for referral to a psychiatric emergency room for youth. Whether there has been an actual increase in such behavior or that police have learned to use psychiatric emergency rooms as disposition sites needs further study.

**References:**


**NR468 Tuesday, May 4, 3:00 p.m.–5:00 p.m.**

**Venlafaxine Extended Release in Children and Adolescents With Social Anxiety Disorder Supported by Wyeth Pharmaceuticals**

Karen A. Tourian, M.D., Wyeth Research, P.O. Box 42528, Philadelphia, PA 19101–2538; John S. March, M.D., Richard Mangano, Ph.D.

**Educational Objectives:**

At the conclusion of this presentation, the participant should be able to discuss: (1) the effects of venlafaxine ER on the symptoms of social anxiety disorder (SAD) in children and adolescents; (2) and compare the efficacy and safety of venlafaxine ER with placebo in the treatment of SAD in children and adolescents.

**Summary:**

**Objective:** To study the efficacy and safety of venlafaxine ER (extended release) in children and adolescents with social anxiety disorder (SAD).

**Method:** 293 subjects aged 8 to 17 years were recruited for a 16-week outpatient study of double-blind, placebo-controlled venlafaxine ER (flexible dose; range determined by weight). Subjects had a DSM-IV diagnosis of social phobia (social anxiety disorder), a Social Anxiety Scale (SAS) score ≥50, and a CGI-S Severity score ≥4. A diagnosis of major depressive disorder or a CDRS score ≥40 were exclusionary.

**Results:** The primary outcome variable was the SAS Child or Adolescent version. In the intent-to-treat population, with last observation carried forward, there was a statistically significant improvement of subjects taking venlafaxine ER compared with placebo from week 3 on, with adjusted mean scores at week 16 final on-therapy of 42.95 vs. 50.60 (P<0.001). There were no suicides or suicide attempts. Safety findings comparable with previous venlafaxine ER pediatric studies.

**Conclusions:** Venlafaxine ER may be an effective treatment for children and adolescents with SAD who do not have major depressive disorder. Physicians should be alert to signs of suicidal ideation in child and adolescent patients taking venlafaxine ER.

**Funding Source(s):** Wyeth Research

**References:**

creased to a final on-therapy mean CDRS-R total score of 24.3 at month 6 (Observed Cases; 33.8 on LOCF). The percentage of patients responding to treatment, as measured by the CDRS-R total, HAM-D total, and CGI-I scores, increased over time. The most common treatment-emergent adverse events were headache (53%), nausea (26%), infection (24%), abdominal pain (22%), vomiting (21%), and pharyngitis (19%). Two venlafaxine-treated patients had hostility, and 2 patients had suicide attempts, which all lead to discontinuation from the study. There were no suicides in this study.

Conclusion: Long-term treatment with venlafaxine ER was associated with progressive improvement over time. Prescribers should be alert to signs of suicidal ideation in pediatric patients taking venlafaxine.

Funding Source(s): Wyeth Research

References:

NR470 Tuesday, May 4, 3:00 p.m.-5:00 p.m.
Efficacy and Safety of Venlafaxine Extended Release in Children and Adolescents With MDD Supported by Wyeth Pharmaceuticals
Graham J. Emslie, M.D., Children’s Medical Center, 1935 Motor Street, Dallas, TX 75235; Robert L. Findling, M.D., Paul P. Yeung, M.D., Nadia R. Kunz, Pharm.D., Yunfeng Li, Billie L. Durn

Educational Objectives:
At the conclusion of this session, the participant should be able to summarize the effects of atomoxetine in patients with moderate or severe hyperactive or inattentive ADHD symptoms.

Summary:
Objective: Atomoxetine has been shown to be efficacious in numerous placebo-controlled trials in children and adolescents with ADHD. Post-hoc analyses examined the data from five clinical trials to determine the efficacy of atomoxetine in patients who had the most severe symptoms at baseline.

Methods: Patients were classified as having moderate symptoms if their baseline ADHD Rating Scale T-scores were greater than 1.5 standard deviations above age and gender norms (T > 65) and having severe symptoms if T-scores were greater than 3 standard deviations (T > 80). Treatment differences in change from baseline for Total and subscale scores were compared using ANCOVA.

Results: There were 674 patients (atomoxetine n=399, placebo n=275) who had moderate hyperactive symptoms at baseline and 815 patients (atomoxetine n=480, placebo n=335) who had moderate inattentive symptoms at baseline. There were 339 patients (atomoxetine n=210, placebo n=129) who had severe hyperactive symptoms at baseline and 444 patients (atomoxetine n=277, placebo n=167) who had severe inattentive symptoms at baseline. Among both moderately and severely impaired patients, significant improvement was noted with atomoxetine treatment compared with placebo treatment (all p-values’s <.001, effect sizes=.6-.9).

Conclusion: These analyses indicate that atomoxetine is beneficial for treating patients with moderate or severe hyperactive or inattentive symptoms.

Funding Source: Eli Lilly and Company

NR471 Tuesday, May 4, 3:00 p.m.-5:00 p.m.
Atomoxetine Efficacy for Severe Hyperactive and Inattentive ADHD Symptoms Supported by Eli Lilly and Company
Jeffrey Newcom, M.D., Psychiatry Department, Mt. Sinai Medical Center, 1425 Madison Avenue, Room 4-40, New York, NY 10029; Virginia Sutton, Ph.D., Calvin R. Sumner, M.D., Douglas K. Kelsey, M.D., Kory Schuh

Educational Objectives:
At the conclusion of this session, the participants should be able to summarize the effects of atomoxetine in patients with moderate or severe hyperactive or inattentive ADHD symptoms.

Summary:
Objective: Atomoxetine has been shown to be efficacious in numerous placebo-controlled trials in children and adolescents with ADHD. Post-hoc analyses examined the data from five clinical trials to determine the efficacy of atomoxetine in patients who had the most severe symptoms at baseline.

Methods: Patients were classified as having moderate symptoms if their baseline ADHD Rating Scale T-scores were greater than 1.5 standard deviations above age and gender norms (T > 65) and having severe symptoms if T-scores were greater than 3 standard deviations (T > 80). Treatment differences in change from baseline for Total and subscale scores were compared using ANCOVA.

Results: There were 674 patients (atomoxetine n=399, placebo n=275) who had moderate hyperactive symptoms at baseline and 815 patients (atomoxetine n=480, placebo n=335) who had moderate inattentive symptoms at baseline. There were 339 patients (atomoxetine n=210, placebo n=129) who had severe hyperactive symptoms at baseline and 444 patients (atomoxetine n=277, placebo n=167) who had severe inattentive symptoms at baseline. Among both moderately and severely impaired patients, significant improvement was noted with atomoxetine treatment compared with placebo treatment (all p-values’s <.001, effect sizes=.6-.9).

Conclusion: These analyses indicate that atomoxetine is beneficial for treating patients with moderate or severe hyperactive or inattentive symptoms.

Funding Source: Eli Lilly and Company
NR473 Tuesday, May 4, 3:00 p.m.-5:00 p.m.
Long-Term Efficacy and Safety of Risperidone in Children With Disruptive Behavior Disorders: Two Years of Data
Supported by Johnson & Johnson
Magali Reyes-Harde, Ph.D., Pharmaceutical Research and Development, Johnson and Johnson, 1125 Trenton-Harborton Road, Titusville, NJ 08530; Jan Croonenberghs, M.D., Marielle Eerdekens, M.D., Roza Oolah, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize that risperidone remains safe and effective during long-term treatment of children with conduct disorders and below-average IQs.

Summary:
Objective: To assess long-term safety and efficacy of risperidone in children with conduct (CD), oppositional defiant (ODD) and disruptive behavior disorder not otherwise specified (DBD-NOS).

Method: This international, open-label study, an extension to a larger one-year trial, followed 48 children, aged 7–15 years with below-average IQ (35–84) and comorbid ADHD. Risperidone was administered for 24 months following a one-year open-label safety study. Safety was assessed by the Extrapyramidal Symptom Rating Scale (ESRS), adverse events, clinical laboratory tests, vital signs, BMI, and ECG. Efficacy was measured by the Clinical Global Impression (CGI) score.

Results: The mean dose of risperidone was 1.92 mg/day (range 0.6–3.17). Symptoms continued to be well controlled in these children as measured on the CGI (mean 3.1 [mild] decreased from 5.6 [severe]). Risperidone was well tolerated during long-term administration. Few extrapyramidal side effects occurred as assessed by the ESRS. The children showed a modest increase in BMI, which was within the range of age appropriate expected growth. There were no clinically significant changes in ECG parameters.

Conclusions: Continuing low dose treatment with risperidone over three years was well tolerated, safe and effective in children with DBDs.

References:

NR472 Tuesday, May 4, 3:00 p.m.-5:00 p.m.
Role of the Implicit Theories of Intelligence on Cognitive Tasks
David da Fonseca, Sainte Marguerite Hospital, Marseille 13009, France; Francois Cury, Daniel Bailly, Marcel Rufo

Educational Objectives:
At the conclusion of this session, the participant should be able to determine motivational factors involved in achievement situations in order to explain maladaptive behavior in academic situations.

Summary:
The aim of this study was to demonstrate that it was possible to modify experimentally implicit theories of intelligence, cognitions, and behaviors by modifying situational factors. So we have compared the effect of the induction of an implicit theory of intelligence (entity theory vs. incremental theory) on cognitive task. Four groups of 25 adolescents have been exposed to one of the four experimental conditions. The results show that:
• the incremental theory induction (in which intelligence is believed to be malleable) with a positive or negative feedback leads to a high score of perseverance and a low score of anxiety.
• the entity theory induction (in which intelligence is believed to be a fixed characteristic) with a negative feedback leads to a high score of anxiety and a low score of perseverance.
• the entity theory induction with a positive feedback leads to a weak score of anxiety and perseverance. The results demonstrate that participants in incremental condition obtained better performance than those in entity condition. These results should lead to plan programmes of cognitive therapy in order to modify beliefs of adolescents with learning disabilities.

References:

Reference:

Results: The mean dose of risperidone was 1.83 mg/day (range 1.44–3.89). Nearly equal numbers of children and adolescents were enrolled. NCBRF scores continuously improved from a baseline mean of 32.3 (SD 7.1) to a mean of 12.8 (SD 8.51) after two years of treatment. The incidence of adverse events decreased during the second year of treatment. A modest increase in BMI (0.3 kg/cm²) was observed in the second year, which was within the range of age-appropriate expected growth. There were no cases of TD.

Conclusion: These are the only data available addressing long-term administration of antipsychotic medication to children with DBDs. Risperidone was well tolerated, safe and effective during two years of treatment.

Funding Source(s): Janssen Pharmaceutica Products, LP

References:

NR475	Tuesday, May 4, 3:00 p.m.–05:00 p.m.
Effect of Atomoxetine in Treating Pediatric ADHD in a Natural Setting
Supported by Eli Lilly and Company
Calvin R. Sumner, M.D., Neuroscience, Eli Lilly and Comp, Lilly Corporate Center DC4135, Indianapolis, IN 46285; Douglas K. Kelsey, M.D., Virginia Sutton, Ph.D., Sandra Malcolm, Ph.D., Rosalie Bakken, Ph.D.

Educational Objectives:
At the conclusion of this session, participants should be able to summarize the effectiveness of atomoxetine in treating children and adolescents with ADHD in a naturalistic setting.

Summary:
Objective: The effectiveness of atomoxetine, a nonstimulant medication indicated for treatment of ADHD, was evaluated in pediatric and adolescent patients, as measured by the Physician Global Impression: ADHD Severity (PGI-ADHD-S) and patient reports.

Methods: In this non-interventional, prospective, observational, longitudinal, open-label study, acute interim data from 482 patients were collected during routine physician visits. Drug administration and dosing were at the physician's discretion.

Results: Results of the PGI-ADHD-S (a seven-point scale) show a significant reduction in ADHD severity relative to baseline (mean change in score and 95% CI = 0.8, 0.66–0.89; p<0.001). Mean scores improved significantly among subgroups with comorbid conditions including anxiety, tics/Tourettes, and oppositional-defiant disorder. Most patients experienced consistent symptom control throughout the morning, daytime, and evening hours. The majority of patients reported that grades improved or stayed the same and that behavior and family interactions improved. Those previously treated with stimulants experienced significant improvement on atomoxetine, and few patients discontinued the study.

Conclusion: This is the first systematic study of atomoxetine treatment for ADHD in community practice. Results indicate that atomoxetine is effective and well-tolerated by children and adolescents, as measured by physician and patient reports, corroborating the favorable results of clinical trials.

Funding Source: Eli Lilly and Company

References:

NR476	Tuesday, May 4, 3:00 p.m.–05:00 p.m.
Low Rate of Movement Disorders in Risperidone-Treated Pediatric Patients
Supported by Janssen Pharmaceutica and Research Foundation
Cynthia Bossie, Ph.D., Janssen Pharmaceutica Products, L.P., 1125 Tranton-Harbourton Road, Titusville, NJ 08560; Georges Gharabawi, M.D., Young Zhu, Ph.D., C. Rick Jarecke, Pharm.D., Gahan J. Pandina, Ph.D.

Educational Objectives:
At the conclusion of this presentation, participants should be able to recognize the effects of risperidone on tardive dyskinesia and movement disorders in pediatric patients with disruptive behavior disorders.

Summary:
Objective: Few studies have assessed the effects of atypical antipsychotics on movement disorders in pediatric patients, although data suggest they have a reduced potential for inducing extrapyramidal symptoms. Acute and tardive movement disorders were assessed in pediatric patients with disruptive behavior disorders (DBDs) receiving risperidone.

Method: Data were from two one-year, open-label extensions of short-term, placebo-controlled trials, and a third one-year open-label study. Dyskinesia was defined as ≥2 scores of 2–3, or one score of ≥4 on the Extrapyramidal Symptom Rating Scale (ESRS) dyskinesia subscale (E51–E57). Tardive dyskinesia (TD) was defined as dyskinesia at ≥2 consecutive visits in patients without dyskinetic symptoms at baseline (all 7 ESRS dyskinesia items = 0–1). Symptoms were evaluated at baseline, weeks 1–4, 8, 16, 20, 24, 36, 48, and endpoint. Results-Data were available for 683 patients. ESRS scores generally were low. Among the 651 patients without dyskinetic symptoms at baseline, two (0.3%) patients met the predefined TD criteria during the study. Both cases resolved with continued treatment, demonstrating that these were reversible dyskinesia cases. Twelve patients had dyskinesia at baseline; these symptoms decreased at study end.

Conclusions: Risperidone was associated with a low risk of acute movement disorders in pediatric patients with DBDs in three large 1-year studies.

Funding Source(s): Supported by Janssen Pharmaceutica Products, L.P.

References:
NR477  Tuesday, May 4, 3:00 p.m.—05:00 p.m.
Clinic Validation of the MDQ for Adolescents
Supported by GlaxoSmithKline
Karen D. Wagner, M.D., Department of Psychiatry, University of Texas Medical Branch, Room 3.258, 301 University Boulevard, Galveston, TX 77555-0188; Robert M.A. Hirschfeld, M.D., Graham J. Elkins, M.D., Barbara L. Gracious, M.D., Robert L. Finding, M.D., Michael Reed, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should understand the reliability and validity of MDQ for adolescents and the value of parent versus self-reported symptoms in detecting and diagnosing bipolar disorder among adolescents.

Summary:
Objective: To determine reliability and validity of MDQ in detecting bipolar disorder among those aged 12–17.

Methods: Parents and adolescents (n=104) from four outpatient child psychiatry clinics completed the MDQ. Adolescents completed the scale twice, once from their perspective (Self) and again from the perspective of others (Attributional). Diagnostic interviews (K-SADS) were completed for all patients.

Results: Forty patients received K-SADS diagnosis of bipolar disorder, 37 were diagnosed major depressive disorder and the balance received a variety of diagnoses (ADHD, dysthymia, schizophrenia). MDQ internal reliability was strong for self, attributional and parent forms (Cronbach’s-alpha: .84, .84, .83, respectively). Self and attributional ratings were highly correlated (r = .89) but neither correlated as well with Parent ratings (r = .37 and .41, respectively). Parent item ratings correlated strongly with K-SADS (kappa range: .12–.42; p<.05, 11 of 13 items). Parent ratings significantly differentiated (p<.05) bipolar patients from unipolar depressed patients on 11 of 13 items.

Conclusions: Parent, Self and Attributional versions of MDQ have good internal reliability. However, only parent reports correlate with K-SADS. MDQ may be a useful screening instrument for adolescents with bipolar disorders. Bipolar adolescents lack insight into their condition suggesting parent reports from MDQ may prove useful in screening bipolar disorder in this age group.

References:

NR479  Tuesday, May 4, 3:00 p.m.—05:00 p.m.
Open-Label Evaluation of the Safety and Efficacy of Escitalopram in Children and Adolescents With Depression
Supported by Forest Laboratories, Inc.
Karen D. Wagner, M.D., Department of Psychiatry, University of Texas Medical Branch, Room 3.258, 301 University Boulevard, Galveston, TX 77555-0188

Educational Objectives:
At the conclusion of this session, the participant will increase their knowledge about the safety and efficacy of citalopram for the treatment of pediatric depression.

Summary:
Introduction: Citalopram has been shown to be effective in treating pediatric depression. Escitalopram is the therapeutically active component of citalopram, and is indicated for major depressive disorder (MDD) in adults.

Methods: Male and female pediactric outpatients (children 6–11 years, and adolescents 12–17 years) with a diagnosis of MDD (DSM-IV criteria) received eight weeks of open-label, flexible-dosed escitalopram 10–20 mg/day. The primary efficacy measure was the change from baseline Children's Depression Rating Scale-Revised (CDRS-R) score at week 8. Clinical Global Impression of Severity (CGI-S) was a secondary outcome measure. Last-observation-carried-forward (LOCF) results are presented.

Results: Seven children and five adolescents received at least one escitalopram dose. Mean baseline scores were CDRS-R= 60.7 and CGI-S=4.2; children and adolescents had similar base-
line scores. Mean changes from baseline in CDRS-R was $-32.4$ and CGI-S was $-1.9$, at week 8. Escitalopram appeared to be at least as effective in children (mean CDRS-R change at week 8 = $-38.1$) as in adolescents (mean CDRS-R change at week 8 = $-24.4$). Escitalopram was well tolerated with 11 or 12 patients completing all 8 weeks of treatment. Mean daily dose was 15 mg.

**Conclusion:** These results provide preliminary support for the efficacy and tolerability of escitalopram in treating pediatric depression.

**References:**


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**NR480**

**Tuesday, May 4, 3:00 p.m.-5:00 p.m.**

**Remission of ADHD Symptoms With Stimulant Therapy**

**Supported by McNeil Pharmaceuticals**

Laurence L. Greenhill, M.D., Department of Psychiatry, New York State Psychiatric Institute, 9 Country Road, Mamaroneck, NY 10543; George J. Wan, Ph.D., Kimberly M. Cooper, M.S.

**Educational Objectives:**

To investigate the remission of symptoms as a clinically meaningful index of effectiveness in the treatment of attention deficit/hyperactivity disorder (ADHD) and to recognize that remission of symptoms may vary with short-acting or long-acting methylphenidate treatment in children with ADHD.

**Summary:**

**Objective:** To evaluate remission of symptoms in methylphenidate (MPH)-treated children with attention-deficit/hyperactivity disorder (ADHD).

**Methods:** Children with ADHD (N=292), ages 6–12 years, were randomized to once-daily OROS® MPH (n=95), immediate-release (IR) MPH three times a day (tid; n=97), or placebo (n=90) in a double-blind, 28-day trial. Remission rates at end of study (≥50% and ≥70% reduction from baseline on parent-rated IOWA Conners inattention/overactivity (I/O) subscale) were retrospectively analyzed using the last-observation-carryed forward (LOCF) procedure.

**Results:** Remission rates (≥50% cut-off) were 50.5% for OROS® MPH, 36.7% for IR MPH, and 11.9% for placebo (P<0.0001). These rates were 62.3% and 26.7% for OROS® MPH dosages 36-54 mg and 18mg, respectively (P=0.0018). Remission rates (≥70% cut-off) were 22% for OROS® MPH, 12.2% for IR MPH, and 3.6% for placebo (P=0.0009). These rates were 29.5% and 6.7% for OROS® MPH dosages 36-54mg and 18mg, respectively (P=0.015). No significant differences in remission rates for either cut-offs were observed for IR MPH by dosage.

**Conclusions:** Significantly more patients achieved remission of symptoms (≥50% and ≥70% reduction from baseline on IOWA Conners I/O subscale) when treated with once-daily OROS® MPH than with placebo. Significantly higher remission rates were achieved with higher doses of OROS® MPH.

**Funding Source(s):** McNeil Consumer & Specialty Pharmaceuticals

**References:**


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**NR481**

**Tuesday, May 4, 3:00 p.m.-5:00 p.m.**

**MRI Study of the Hippocampus in Childhood and Adolescent Psychoses**

**Supported by Janssen Pharmaceutical**

Mohamed El-Sayed, M.D., Department of Psychiatry, University of North Carolina-Chapel Hill, CB 7160, Chapel Hill, NC 27599; Limmarie Sirich, M.D., Cecil Charles, Ph.D., Guido Cerig, Ph.D., Jeffrey A. Lieberman, M.D., Sarang Joshi, Ph.D.

**Educational Objectives:**

At the conclusion of this session, the participant should be able to: (1) the hippocampal volume difference of youth presenting with moderate to severe psychotic symptoms and their matched controls; (2) recognize the difference in hippocampal volume observed in youth with schizophrenic, affective diagnoses and normal controls.

**Summary:**

**Objective:** This presentation describes the volume alteration of the hippocampus in 29 patients experiencing a childhood and adolescent psychosis relative to 17 healthy comparison subjects.

**Methods:** The patients in this study included 16 individuals with schizophrenia spectrum disorders and 13 with affective disorders. Subjects had a through diagnostic and clinical evaluation using standardized tools and an extensive neurocognitive battery. High-resolution magnetic resonance imaging (MRI) was done on a GE SIGNA Advantage System operating at 1.5T. Measurement of the intracranial volume components (grey matter, white matter and CSF) was performed using computer assisted segmentation. Measurements of the hippocampus were performed using a highly reliable and newly modified large-deformation-based segmentation tool. Sixteen of the subjects were rescanned after two to six months of antipsychotic treatment.

**Results:** Decrease in the total hippocampus volume, co varied for the intra-cranial volume; were observed in the whole psychotic group (5.504±0.678) compared to the healthy controls (5.577±0.501). In patients rescanned after two to six months, the left hippocampus was significantly decreased in volume (p < 0.05) after two to six months of treatment.

**Conclusions:** Patients with childhood and adolescent psychoses had smaller hippocampus than healthy controls.

**Funding Source(s):** ARSAD, NIMH grant RR00046, Egyptian Ministry of Higher Education and Janssen Pharmaceutical.

**References:**


NR482  Tuesday, May 4, 3:00 p.m.-5:00 p.m.
Training Pediatricians as Primary Care Providers in Child Psychiatry
Brian J. McConville, M.D., Department of Psychiatry, Cincinnati Childrens Hospital, 3333 Burnet Avenue, MLC 3014, Cincinnati, OH 45229; Arman K. Danielyan, M.D., Thomas J. Cataganotto, M.D., Sanjeev Pathak, M.D., Lawrence Lindeman, M.S.W., Karla Morgan, R.N.

Educational Objectives:

At the conclusion of this session, participants will recognize the feasibility of academic child psychiatrists training practicing community pediatricians to be primary care providers in child psychiatry, with minimal consultation follow-up. A feasible and standardized model is demonstrated, with efficacy results.

Summary:

Background: Most children and adolescents with chronic psychiatric problems are managed by pediatricians, with inconsistent child psychiatric input.

Objectives: To report preliminary findings from a collaborative model between community pediatricians interested in child psychiatry and child psychiatry consultants.

Methods: Psychiatric, social work, and psychological assessments are done over two sessions in the consultation clinic. Collected standardized data are computer scored and stored, with reports faxed immediately to the pediatrician. Quarterly CME is provided.

Results: 203 patients and their parents have been seen so far. The first 50 cases ranged from 2.5 to 17 years, (mean = 10.2; Caucasian (94%) males (80%). Most frequent diagnoses at referral versus post-assessment were ADHD (39:41), MDD (7:14), Bipolar Disorder (n=14), GAD (3:12), ODD (13:10), and MDD (3:8). 80% had 1 comorbid Axis I diagnosis. Psychotropics prescribed at referral versus post-assessment were psychostimulants (8:12), antidepressants (13:21), atypical antipsychotics (8:12), and mood stabilizers (3:4). 88.7% of parents were strongly positive. Specific psychotherapy was recommended in 32%. Only 16% required subsequent consultations (mean = 2.4), and no hospitalizations followed.

Conclusions: This model provides feasible extended provision of complex child and adolescent psychiatry services via community pediatricians, with minimal follow-up.

References:


NR484  Tuesday, May 4, 3:00 p.m.-5:00 p.m.
Bupropion Versus Citalopram Versus Placebo in Adolescents With Major Depression
Carol A. Glod, Ph.D., Nursing Department, Northeastern University, 210 Robinson Hall, Boston, MA 02115; Arlene Lynch, M.S., Cynthia Berkowitz, M.D., John Hennen, Ph.D., Ross J. Baldessarini, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to understand the comparative effectiveness of antidepressants in the treatment of adolescent depression.

Summary:

Objectives: The purpose of this double-blind, placebo-controlled, randomized, eight-week trial was to compare the efficacy of bupropion and citalopram in adolescent depression.

Methods: Subjects were physically healthy, medication-free outpatients, between the ages of 12–19 years, with a DSM-IV diagnosis of major depressive disorder (MDD) diagnosed based on semi-structured interview (K-SADS-E). Subjects were randomized to bupropion, citalopram, or placebo (1:1:1). Major outcome measure were changes in scores on the Hamilton Depression Rating Scale (HDRS) supplemented with eight items that assessed atypical depressive symptoms between baseline and endpoint. Subjects were monitored weekly for response, worsening depression, suicidal risk, and side effects.

Results: Results are currently available on 18 subjects (6 male, 12 female, mean age=15.5±1.9 years). Baseline HDRS scores...
averaged 20.3±3.7, overall, and did not differ by treatment. Random-effects time series regression analysis revealed a greater decrease from baseline HDRS scores with bupropion than citalopram (x²=3.29, p=.07), with minor differences between bupropion vs. placebo, and citalopram vs. placebo, and with no differences among treatments regarding improvements in atypical symptoms. Weight loss was the most common side effect: in 43% of bupropion-treated, and 29% of citalopram-treated subjects.

Conclusion: These preliminary results suggest that bupropion may be at least as effective as citalopram in the treatment of mild-to-moderate adolescent depression.

Funding Source(s): NARSAD Independent Investigator Award

References:

NR485  Tuesday, May 4, 3:00 p.m.-5:00 p.m.
Antidepressant Trends Among Children Diagnosed With Depression, 1990–2001
Linda L. Robinson, M.S.P.H., Department of Health Policy and Administration, Washington State University, P.O. Box 646510, Pullman, WA 99164; Tracy L. Skaer, David A. Sclar, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to: (1) recognize the upward trend in the diagnosis of depression over the past 12 years among children and adolescents age 5–18 years; (2) understand trends in the types of antidepressants prescribed for the treatment of depression over the past 12 years among children and adolescents age 5–18 years.

Summary:
Objective: Since 1998, the use of selective serotonin reuptake inhibitors (SSRIs) has been advocated as first-line treatment for depression in children and adolescents. This study was designed to discern trends in the prevalence of office-based visits resulting in a diagnosis of depression among children and adolescents age 5–18 years, and trends in the prescribing of antidepressants for its treatment.

Methods: Using data from the National Ambulatory Medical Care Survey, the number and rate of office-based physician visits resulting in a diagnosis of depression (ICD-9-CM codes 296.2–296.36; 300.4; or 311), and the prescribing of antidepressants (by type) were discerned for the years 1990–2001. Trend analysis was conducted using three, four-year time intervals: 1990–93, 1994–97, 1998–01.

Results: Over the time-frame examined, the U.S. population-adjusted rate of office visits documenting a diagnosis of depression increased 2.4-fold, from 12.9 per 1,000 children and adolescents, to 31.1 per 1,000. The percent of patients prescribed an antidepressant increased from 44.4% to 59.3%; receipt of an SSRI increased from 20.7% to 39.7%; and receipt of a tricyclic antidepressant declined from 21% to 2.7%.

Conclusion: These data reveal significant growth in the rate of children and adolescents diagnosed with depression in the U.S., and significant growth in the prescribing of SSRIs for its treatment.

Funding Source(s): 2001 Independent Investigator Award, National Alliance for Research on Schizophrenia and Depression.

References:

NR486  Tuesday, May 4, 3:00 p.m.-5:00 p.m.
Parental Drinking Problem and Their Children's Psychopathology
Oh-In Kwon, M.D., Psychiatry Department, Armed Force Capital Hospital, Yul-dong, Bunidang-gu Seongnam City, Gyeonggi 463-040, Korea; Joung-Sook Ahn, M.D., Jung-Ho Shin, M.D., Gi-Chang Park, M.D., Jun-Kyu Han, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the issue of children of alcoholics.

Summary:
Objectives: We investigated whether 1. parental drinking problem perceived by adolescent and 2. parent—adolescent relationship are associated with adolescent's psychopathology.

Methods: 1141 students from 4 middle, high schools in Wonju city, Kangwon province, Korea were enrolled. Using Children of Alcoholics Screening Test (CAST), we found that 398 students were adolescents of parent with drinking problem, other 743 students a control. Two groups were evaluated for difference of adolescent's psychopathology using Strengths and Difficulties Questionnaire—Self Report (SDQ-5R) and of parent—adolescent relationship using Attitude Toward Parents Questionnaire.

Results: Adolescents of parent with drinking problems had significantly higher score indicating the hyperactivity, emotional symptoms, conduct problems, and peer problems than in the control group. They showed significantly low level of positive attitude toward parent which we found predicted the severity of adolescent's psychopathology.

Conclusion: Therapeutic intervention improving the parent—child relationship will decrease psychopathology of children of alcoholics.

References:

NR487  Tuesday, May 4, 3:00 p.m.-5:00 p.m.
Treatment Modalities for Depression Among U.S. Children and Adolescents
David A. Sclar, Ph.D., Department of Pharmacy, Washington State University, PO Box 646510, Pullman, WA 99164-6510; Linda L. Robinson, M.P.H., Tracy L. Skaer

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the prevalence of depression and the prevalence of single and combination treatment modalities (antidepressants and/or psychotherapy) among children and adolescents age 5–18 years.

Summary:
Objective: To determine the prevalence of single and combination treatment modalities among U.S. children and adolescents age 5–18 years, diagnosed with depression. Treatments include: (1) antidepressant pharmacotherapy alone; (2) psychotherapy alone; (3) the combination; or (4) no treatment.
Materials & Methods: Data from the U.S. National Ambulatory Medical Care Survey (NAMCS) for the years 1998–2001, were used for this analysis. Office-based physician-patient visits documenting a diagnosis of depression (ICD-9-CM codes 296.2—296.36; 300.4; or 311) were extracted from the NAMCS. Treatment modalities utilized in the management of depression are reported as percentiles.

Results: Over the four year time-frame examined, 6,923,040 office visits documented a diagnosis of depression. The most frequent treatment modality was antidepressant pharmacotherapy alone (38.6%). This was followed by the combination treatment of antidepressant pharmacotherapy plus psychotherapy (20.6%). 18.3% of the patients received psychotherapy alone, and 22.5% received no treatment beyond the office-based visit.

Conclusion: The fact that 22.5% of patients received no treatment may reflect problems associated with access to health insurance, the coverage of mental health services under insurance products, geographic distribution of mental health services, and_or decisions reached by patients or guardians.

Funding Source(s): 2001 Independent Investigator Award, National Alliance for Research on Schizophrenia and Depression

References:


NR489  Tuesday, May 4, 3:00 p.m.-5:00 p.m.  Early Childhood Autism Response to Treatment With Risperidone
Roberto E. Chaskel, M.D., Department of Psychiatry, University Nueva Granada, Apartado Aereo 4124, Bogota, Colombia

Educational Objectives:
At the conclusion of this session, the participant should be able to identify the need for early treatment and further research in severely mentally affected autistic children. Participants should also be able to identify the benefits of current medications, particularly risperidone.

Summary:
Objective: Treatment with antipsychotic drugs has been associated with benefits in children with autism. Recent evidence suggests that the benefit of newer antipsychotic is high compared to the risks. The purpose of this research project was to show the benefit of antipsychotic medication in small autistic children.
Method: A prospective study was conducted with 10 outpatients aged 3–5 yrs. Using DSM-IV TR criteria for autistic disorder (299.00) at the outpatient clinic of the psychiatric dept. at the Military Hospital, Bogota, Colombia. Ratings were done by parents, occupational therapists and language therapists. Mean dosage 7.45 mgs. Risperidone.
Results: Mean (SD) age was 4.2 (.8) years and 80% were male. Mean duration of treatment was 12 months. Improvement on the DBC was seen in aloofness, non-speech noises, mood changes, obsessions with activity, band flapping, overactivity, attention, irritability, eye contact, speech, intent of communication, cuddling in seven of the 10 children. In three, the improvement was substantial in the four last items, but not in the others. These three children also showed other items of comorbid mental retardation. Only secondary effect was sleepiness and doses were reduced.
Conclusion: Autistic children benefit from psychopharmacological interventions, even at an early age. Occupational therapists, language therapists and parents see the improvement in social behavior and in the ability of the child to profit more from therapy.

References:

NR490  Tuesday, May 4, 3:00 p.m.-5:00 p.m.  Aggression in Children With Disruptive Behavior Disorders
Supported by Janssen Pharmaceutica and Research Foundation
Carin Binder, M.B.A., Research Department, Janssen Ortho Incorporated, 19 Green Belt Drive, Toronto, ON M3C 1L9,
NR491 Tuesday, May 4, 3:00 p.m.-5:00 p.m.
Psychotropic Use in Hospitalized, Very Young Children
Sanjeev Pathak, M.D., Children’s Hospital Medical Center, 3333 Burnet Avenue, D3014, Cincinnati, OH 45229-3039; Sarah Arszman, B.A., Arman K. Danielyan, M.D., Erin Johns, B.A., Alex Smimov, M.D., Robert A. Kowatch, M.D.

Educational Objectives:
At the conclusion of this session, the participant should have an awareness of the use of novel antipsychotics for aggression associated with disruptive behaviors in children.

Summary:
Objective: Analyze effect of risperidone on core symptoms of aggression in children.

Methods:
Two, 6-week, double-blind, placebo controlled trials were conducted for analysis on 166 boys. Inclusion: sub-average intelligence, 5-12 years, DSM-IV conduct disorder (CD) or oppositional defiant disorder (OD), score >=24 on conduct problem subscale of the Nisonger Conduct Behavior Rating Form (NCBRF).

Results:
Analyses indicated no consistent relationship between treatment response over time and hypothesized predictor variables.

Conclusion:
Risperidone was effective in treating core aggression symptoms over 6 weeks compared to placebo. Risperidone appears to have an effect on aggression independent of other measures of behavioral and emotional deviance and effect does not appear to be related to diagnosis, age, or IQ.

References:

NR492 Tuesday, May 4, 3:00 p.m.-5:00 p.m.
Valproate in Child/Adolescent Bipolar Disorder: A Comprehensive Meta-Analysis Supported by Abbott Laboratories
Lee S. Cohen, M.D., Department of Psychiatry, Columbia University, Roosevelt Hospital, 623 Warburton Avenue, Hastings, NY 10706; Kim Ching, B.S.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the potential benefits of valproate in child and adolescent bipolar disorder without seizure disorder. The participant will gain a comprehensive evidence base of all the literature examining the use of this compound in youth 18 years of age or younger.

Summary:
The diagnosis of bipolar disorder is a commonly utilized diagnosis in clinical child and adolescent psychiatry today. As compared with adults, children and adolescents with this diagnosis are more likely to present with rapid cycling or mixed states making proper recognition difficult. Furthermore the issue of high levels of comorbid diagnoses increases the management difficulties associated with these youth. Those youth diagnosed with bipolar disorder often have courses of long duration and low recovery rates. Higher rates of relapse as well as the potential risk of suicidal behavior all factor into the difficulty managing these children and adolescents.

Divalproex (DVP) or sodium valproate is one of the most commonly used medications in child/adolescent psychiatry for the diagnosis of cycling mood disorders as well as other conditions such as impulsive/aggressive behavior, conduct disorder, oppositional defiant disorder, schizoaffective disorder, depression and others. However, well controlled studies in the population of children and adolescent patients with bipolar disorder are not currently available in the literature despite the widespread use of this compound.

To further investigate the evidence base behind the use of this compound in child/adolescent psychiatry we have completed the first critical review and meta-analysis of the literature dealing with bipolar children and adolescents with and without seizure disorder who have been exposed and studied with the compound DVP.

References:
Of the initial 46 articles reviewed via a PubMed literature search, nine viable studies met inclusion criteria for valproate use (mean VPA level=86.85 +/-30.65 mcg/ml) in bipolar disorder without epilepsy representing a total of 128 cases of youth 18 years of age or younger exposed to this compound. 92 cases or 72% of the cases identified had a positive response defined by structured assessment scales (YMRS, MMRS, SCID, and OAS). There were no studies on the use of valproate in bipolar children with comorbid seizure disorder that met inclusion criteria. This meta-analysis demonstrate the potential positive benefit of Valproate in children and adolescents with bipolar disorder without seizure disorder. Of note is the absence of any large scale double blind placebo controlled trials examining this compound in youth. Based on this data set Valproate should be further investigated in well controlled trials to clearly delineate its' efficacy and safety in child and adolescent psychiatric patients.

**Funding Source(s):** Abbott H. Laboratories

**References:**


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NR493 Tuesday, May 4, 3:00 p.m.-5:00 p.m.

Ziprasidone in Adolescent Neuropsychiatric Patients: Efficacy and Safety

Lee S. Cohen, M.D., Department of Psychiatry, Columbia University, Roosevelt Hospital, 623 Warburton Avenue, Hastings, NY 10706; Emily J. Blaine, Laura DiGiovanni

**Educational Objectives:**

At the conclusion of this session, the participant should be able to recognize the risk/benefit ratio of ziprasidone in child and adolescent patients manifesting impulsive, aggressive and self injurious behaviors. The participant will gain an understanding of the cardiovascular response of children and adolescents exposed to this compound. The participant will learn about clinical response data in neuropsychiatric child and adolescent patients on Ziprasidone.

**Summary:**

Currently atypical antipsychotics are regularly used in child and adolescent populations for psychotic illnesses as well as mood disorders, disruptive behavioral disorders, pervasive developmental disorders, tics and other conditions. Issues regarding efficacy and safety of these compounds in children remain unclear since the literature in child/adolescent populations regarding the use of these agents is limited.

This study examines the efficacy and cardiovascular safety of ziprasidone in neuropsychiatrically ill adolescents on an outpatient basis. 13 consecutively treated neuropsychiatric patients in our outpatient clinic were examined for response to ziprasidone and for cardiovascular safety. Patients manifested a mean age of 13.62 (range 9-21 years) and were exposed to a mean dose of 83.08 mg/day of ziprasidone with a range of 40-120 mg/day. Average length of time treated with ziprasidone was 134.5 days. Patients had the following primary diagnoses: 5 pervasive developmental disorder NOS, 3 autistic disorder, 1 Asperger's disorder, 1 ADHD NOS, 1 conduct disorder, and 2 oppositional defiant disorder. Clinical Global Impressions Severity of Illness at start of the study was a mean score of 5.62 (markedly-severely ill). Mean value of CGI Global Improvement at endpoint was 1.77 (much-very much improved). 11 of 13 patients were rated much improved or very much improved after clinical review by a board certified child psychiatrist.

Cardiovascular safety was examined via clinical reports and serial EKG's done at baseline and at 20-40mg dose increases of ziprasidone. Analysis was then conducted to examine pulse rate and interval changes on EKG at baseline and endpoint after maximum dosage exposure to ziprasidone. Mean Start EKG values were as follows: Vent rate=80.23 bpm, PR int=147.38 ms, QRS duration=87.38 ms, QT/QTc 352.00/407.92 ms. Mean End EKG values were as follows: Vent rate=77.77 bpm, PR int=152.77. QRS duration=87.85 ms, QT/QTc=367.54/409.69 ms. There were no clinical reports of cardiovascular related adverse events. Analyses of all EKG values using t test indicated no significant change in ventricular rate or any EKG parameters with the following data: Vent rate: t(13) = 0.812, p>.05 (p=.433). PR Interval: t(13) = -1.785, p>.05 (p=.099). QRS duration: t(13) = -0.454, p>.05 (p = .658). QT: t(13) = 1.899, p>.05 (p=.082). QTc: t(13) = -0.416, p>.05 (p=.685).

This expanded pilot study indicates that 85% of adolescents treated with ziprasidone as monotherapy(n=5) or as adjunctive treatment(n=8) manifested much or very much improvement on CGI global improvement. No significant cardiovascular adverse reactions were seen with cardiac monitoring. Ziprasidone is a potentially useful agent for neuropsychiatrically ill children and adolescents on an outpatient basis. Further controlled studies are warranted in child and adolescent populations to further delineate this compounds usefulness and safety in this age range.

**References:**


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NR494 Tuesday, May 4, 2004, 3:00 p.m.-5:00 p.m.

Reliability and Validity of the Korean Version of the Preschool Temperament and Character Inventory

Jin-Kyun Park, M.D., Department of Psychiatry, Konyang University, 685 Gasoowon-Dong Seo-Gu, Daejeon 302-718, Korea; Ji Woong Kim, M.D., Seon Wan Kee, M.D.

**Educational Objectives:**

At the conclusion of this session, the participant should be able to recognize the validity of application of the seven-factor model of personality to early childhood and evaluate the reliability and validity of the Korean version of the preschool TCI.

**Summary:**

The purpose of this study was to evaluate the reliability and validity of the Korean version of the preschool Temperament and Character Inventory(K-psTCI), a questionnaire based on Cloninger's seven-factor model of personality. The psTCI was translated into Korean and administered to 266 children aged 2-6 years. A test-retest study of the K-psTCI was conducted across a 4-month interval. Internal consistency was calculated by Cronbach α. Test-retest reliability was analyzed by Pearson correlation analysis. Factor analyses for the temperament and character dimensions were performed using principal component analysis, rotating factors by varimax. A comparison of psTCI scores between Korean and United States preschoolers was done. Cronbach α values for the K-psTCI scales ranged from .62 to .78 for each dimensions. Test-retest correlations (r) ranged from .50 to .77 for each dimensions. Explorative factor analysis with a condition of eigenvalue greater than 2 produced four factors for the temperament items
and three factors for the character items like the US original version of psTCI. Through factor analyses, Five items in the K-psTCI were categorized differently from the US version of psTCI. Korean preschoolers had higher mean scores on Cooperativeness in males as compared to a sample of US preschoolers. The results of this study confirm that the Korean preschool TCI has satisfactory reliability and validity.

References:

NR495 Tuesday, May 4, 3:00 p.m.-5:00 p.m.
Regional Cerebral Perfusion Abnormality in Autism: A SPECT Study

Kwang-Mo Chung, M.D., Department of Psychiatry, Seoul National University, 28 Yongdongdaeho-ro, Seoul 110-744, Korea; Boongyun Kim, M.D., Minseop Shin, Ph.D., Kangeui Hong, M.D., Dongsoo Lee, M.D., Soochuri Cho, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize a defect in the frontal lobe and cerebellum is an important finding in the neural basis of autistic disorder.

Summary:
Objective: Autistic disorder is a well-known psychiatric disorder that has a neural base. To investigate the underlying neurofunctional abnormalities of autism, the authors performed a voxel based imaging study of cerebral blood flow.

Methods: 31 Children with untreated autistic disorder were selected among the patients visiting a child and adolescent psychiatric clinic of Seoul National University Hospital. They were assessed with DSM-IV criteria of autistic disorder, psychometric tool, neuropsychological battery. Moreover, only whenever two psychiatrists independently agreed on the assessment, they were included in the autistic group. All patients were examined by using 99m TC-HMPAO Brain SPECT. Using SPM analysis, we compared SPECT image of autistic patients and standardized SPECT image of normal children, that was developed by our team during 3 years, on a voxel by voxel basis using t-statistics. Voxels with a p-value of less than 0.001 were considered to be significantly different.

Results: The autistic group had a significant decrease of cerebral blood flow in both medial frontal lobe, both cingulated gyrus, both cerebellum, both precuneus gyrus. In addition, they had a significant hyperperfusion in both inferior occipital and parietal lobes, both precentral gyrus, both fusiform gyrus.

Conclusion: The results confirm the presence of functional defects in medial-frontal lobe, cingulated gyrus, cerebellum that have been already reported. So, they are compatible with a recently suggested ‘theory of mind’ hypothesis and a earlier suggested disturbances in cerebro-cerebellar network. Hyperperfusion findings in some area is not reported until now, so further study is required.

References:

NR496 Tuesday, May 4, 3:00 p.m.-5:00 p.m.
Effects of Atomoxetine and Methylphenidate on Sleep in Children With ADHD Supported by Eli Lilly and Company
Virginia Sutton, Ph.D., Department of Neuroscience, Eli Lilly and Company, 9804 Spire Lane, Plano, TX 75025; Rahul Sangal, M.D., Judith Owens, M.D., Albert J. Allen, M.D., Douglas K. Kelsey, M.D., Kory Schuh

Educational Objectives:
At the conclusion of this session, participant should be able to summarize the effects atomoxetine and methylphenidate have on sleep in children with ADHD.

Summary:
Objective: Atomoxetine is a nonstimulant medication for treating ADHD. This study compared the effects of atomoxetine and methylphenidate on the sleep of children with ADHD as measured by actigraphy, polysomnography, and parent and child diaries.

Methods: The study was a randomized, double-blind, crossover trial. After collecting baseline measures, patients were treated with each medication for about seven weeks. Parents and patients completed diaries, patients wore wrist actigraphy monitors, and polysomnography data were collected.

Results: Relative to baseline, the actigraphy data indicated that methylphenidate increased time to sleep onset significantly more than atomoxetine (30.14 versus 3.36 min, p<.001). This was consistent with the polysomnographic data. Child diaries indicated that it was easier to get up in the morning, it took less time to fall asleep, and they slept better with atomoxetine. Parents reported that it was less difficult getting their children up and getting them ready in the morning and they were less irritable, children had less difficulty getting ready for bed, and had less difficulty falling asleep with atomoxetine.

Conclusion: The main finding was that patients on atomoxetine reported shorter time to sleep onset and more normal sleep relative to methylphenidate as measured by actigraphy, polysomnography, child diaries, and parent diaries.

Funding Source: Eli Lilly and Company

References:

NR497 Tuesday, May 4, 3:00 p.m.-5:00 p.m.
Elevated Prolactin Levels in Children and Adolescents Treated With Risperidone and Quetiapine
Paul I. Kymissis, M.D., 110 Lake Drive, Manhasset, NY 11040-1137, Jonathan R. Stevens, B.A., Amy J.L. Baker, Ph.D.
Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the prevalence of hyperprolactinemia in children and adolescents treated with atypical antipsychotics.

Summary:

The aim of this study is to report on the serum prolactin levels in 70 male youth at a residential treatment center treated with either risperidone or quetiapine. This is a cross-sectional retrospective medical chart review of 50 males (mean age, 13.0 ± 2.2 years) treated with risperidone (mean dose, 2.4 ± 1.6 mg/day) and 20 males (mean age, 13.6 ± 2.3 years) treated with quetiapine (mean dose, 317.5 ± 238 mg/day). Serum prolactin levels were drawn according to a protocol, after at least 6 weeks of treatment. Prolactin was increased above the upper limit of normal for 68% of the patients on risperidone and 20% of the patients on quetiapine (chi2 analysis: R=Q, p<0.001). Both risperidone and quetiapine produced dose-related increases in serum prolactin levels (R, r=0.34 p<0.016; Q, r=0.48 p<0.03). Duration of treatment was not associated with prolactin levels. Given the potential adverse effects of hyperprolactinemia in young patients—including growth arrest and sexual dysfunction—periodic monitoring of prolactin during treatment with atypical antipsychotics may be warranted in order to maintain treatment safety in this population.

References:


Behavioral Benefits With Continued Donepezil Treatment in Alzheimer’s Disease Patients Supported by Eisai, Inc. and Pfizer, Inc.

Harald Hampel, M.D., Ludwig-Maximilian University, Nussbaumstg 7, Munich 80336, Germany; Peter Johannsen, M.D., Rachel Schindler, M.D., Elliot Schwam, Ph.D., Yi Kang Xu, Ph.D., Richard F. Holug, M.D., Soren Jakobsen, M.D., Iwoma Kloszewska, M.D., A. Sakka, M.D., Eric Salmon, M.D., Matyas Trixler, M.D., Frans Verhey, M.D., Susanne Qvitzau, M.D., Sharon Richardson, Ph.D.

Educational Objectives:

At the conclusion of this session, participants should be able to identify the importance of behavioral symptoms after administering donepezil to patients with mild-to-moderate Alzheimer’s disease.

Summary:

Background: Donepezil provides benefits across the severity spectrum of Alzheimer’s disease (AD), but is often discontinued in patients whose cognition declines.

Objective: To examine benefits of continued treatment in AD patients who, during initial therapy, showed uncertain benefit.

Methods: The AWARE study enrolled patients with mid-to-moderate AD and included a 24-week, open-label donepezil (10 mg/day) treatment phase, a 12-week, randomized, double-blind phase (continued donepezil or placebo) for patients showing uncertain benefit, and a 12-week, single-blind donepezil treatment phase. Behavior during double-blind treatment was assessed on the Neuropsychiatric Inventory (NPI). Results are reported for intent-to-treat observed cases.

Results: Following open-label treatment, patients showing uncertain benefit (n=202) were randomized to receive donepezil (n=99) or placebo washout (n=103) NPI scores ranged from 0–50 at baseline. Behavioral symptoms improved in patients receiving continued donepezil, compared with decline in patients receiving placebo, and this difference was significant (least squares mean change from NPI baseline score at Week 12: donepezil, –2.60 placebo, 0.78±1.03; P=0.0171).

Conclusions: AD patients who continued on donepezil demonstrated significant behavioral benefits over those who switched to placebo. Behavioral symptoms should be considered an important clinical outcome measure when evaluating treatment responses in AD patients.

Funding Source(s): Eisai Inc, Pfizer Inc.

References:


Changes in Long-Term-Care Residents Continuing or Discontinuing Donepezil Supported by Pfizer Inc.

Sonali N. Shah, R.Ph., Outcomes Department, Pfizer Inc., 235 East 42nd Street, New York, NY 10017; Denis Kechane, Billy D. Strunk, Blaise Mercadante, Ph.D., Tom McRae, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to understand the cognitive, functional, and behavioral benefits of continued donepezil treatment in patients with Alzheimer’s disease in the long-term care setting.

Summary:

Objective: To compare the characteristics of long-term care residents diagnosed with Alzheimer disease (AD) continuing versus discontinuing donepezil treatment.

Methods: Patient data were collected retrospectively using the Minimum Data Set (MDS). Baseline MDS was completed within the first 60 days of donepezil treatment. For the discontinuing cohort. The second MDS was completed at least 90 days after discontinuation of donepezil in the continuing cohort, the second MDS assessment was completed between 8–12 months following the index date of treatment with donepezil. Propensity matching was conducted to match cohort groups.

Results: Continued donepezil treatment (n=210) significantly improved behavior frequency and alterability, quality of life (QoL), and falls over baseline assessments. Discontinuation of donepezil (n=210) resulted in statistically significant declines in cognitive status functional mobility, and increased average daily labor costs from baseline assessments. The number of episodes of urinary incontinence increased significantly for both groups but was higher for the discontinuing group. Accidental falls decreased for both groups compared to baseline. Comparison of treatment groups showed statistically significant differences in measures of cognition, functional mobility, continence, QoL, and average daily labor cost.

Conclusion: Persistence with donepezil treatment improved cognitive, functional, and behavioral outcomes and saved labor costs.

References:


NR500
Tuesday, May 4, 3:00 p.m.-5:00 p.m.
Donepezil Sustains Cognitive Improvements for One Year in Vascular Dementia Patients
Supported by Eisai, Inc.

Holly Posner, M.D., Eisai Medical Research Inc., 500 Frank W. Burr Boulevard, Teenanck, NY 07668-6741; Carlos A. Perdomo, M.S., Raymond D. Pratt, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to: (1) identify long-term treatment benefits in vascular dementia patients; and (2) recognize the importance of long-term donepezil therapy for vascular dementia.

Summary:
Background: Donepezil treatment provides cognitive and global function benefits in patients with vascular dementia (VaD) for at least six months.
Objective: To investigate long-term (1-year) efficacy and tolerability of donepezil in VaD patients.
Methods: This was an open-label, 30-week extension. Patients diagnosed with VaD (National Institute of Neurological Disorders and Stroke and the Association Internationale pour la Recherche et Enseignement en Neurosciences criteria), who completed one of two double-blind, placebo-controlled, 24-week studies with donepezil, were enrolled. Patients received donepezil 5 mg/day for six weeks, optionally increased to 10 mg/day. Results for Week 30 observed cases (54 weeks total) are reported as mean change from double-blind baseline scores for patients receiving 54 weeks of continual therapy.
Results: 885 patients were enrolled. Of the 584 patients randomized to 24 weeks of double-blind treatment, 453 (78%) completed 30 weeks of additional open-label donepezil treatment (64 weeks of continual therapy). Withdrawals due to adverse events were low (n=78; 14%). Patients receiving donepezil sustained their improvement in Alzheimer’s Disease Assessment Scale-cognitive subscale scores after 54 weeks (5 mg/day, −1.15±0.39; 10 mg/day, −0.51±0.37).
Conclusions: Patients receiving continuous donepezil treatment maintained cognitive improvements for 12 months, supporting long-term efficacy and safety of donepezil in VaD patients.
Funding Source(s): Eisai Inc.

References:

NR501
Tuesday, May 4, 3:00 p.m.-5:00 p.m.
Five-Year Effects of Rivastigmine on Cognitive Performance
Supported by Novartis Pharmaceuticals Corporation

Mary Sano, Ph.D., Bronx DVA Hospital, 130 W. Kingsbridge Road, #1FO1, Bronx, NY 10468; Jacques Touchon, M.D., Peter Quarg, Ph.D., Gordon Graham, Ph.D., Rene Spiegel, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should learn about the planning and execution of weight reduction program in inpatient setting and gain insights into effective weight management strategies for chronically mentally ill.

Summary:
Objective: To evaluate the effects of rivastigmine (an inhibitor of AChE and BuChE) on Alzheimer’s Disease Assessment Scale cognitive subscale (ADAS-cog) scores in Alzheimer’s disease (AD) patients over five years.
Methods: Patients completing four randomized, placebo-controlled, 26-week rivastigmine studies were invited to continue open-label rivastigmine for up to five years. The databases were pooled and ADAS-cog scores calculated. An algorithm projected cognitive decline, had patients been left untreated. Results were confirmed with bias-adjusted analyses. Findings were related to assessments made with the Global Deterioration Scale (GDS).
Results: Of 2,010 participating patients, 1988 provided ADAS-cog data. The mean (SD) ADAS-cog score at baseline was 24.6 (12.4). ADAS-cog scores corresponding to moderate (GDS 4), moderately severe (GDS 5) and severe (GDS 6) dementia were 23, 33, and 45, respectively. Model-based untreated patients reached ADAS-cog scores corresponding to moderately severe and severe AD at 1.5 and three years, respectively, while rivastigmine-treated patients were maintained below these thresholds for 2.5 and five years. We investigated a number of potential sources of bias and found they did not significantly affect overall results.
Conclusion: Rivastigmine stabilized patients remaining on rivastigmine treatment for up to five years, delaying deterioration to severe dementia by at least two years.
Funding Source(s): Novartis

References:

NR502
Tuesday, May 4, 3:00 p.m.-5:00 p.m.
Building My Image: A Behaviorally Oriented Program for Reducing BMI

Kachigere Krishnappa, M.D., Psychiatry Department, Capital District Psy C.T., 75 New Scotland Avenue, Albany, NY 12208; Panakkal David, M.D., Joan Pettis, Gerald Engel, R.Ph., John Herasimchuck, M.S.

Educational Objectives:
At the conclusion of this session, the participant should learn about the planning and execution of weight reduction program in inpatient setting and gain insights into effective weight management strategies for chronically mentally ill.

Summary:
Weight gain in chronically mentally ill with increased use of atypical antipsychotics has become a central issue in treatment. However, there is a paucity of published articles using behavioral management techniques.
We present a model for change and data from an eight-month, naturalistic, open-label study incorporated into a state hospital’s daily activities. Thirty patients with Body Mass Index (BMI) above 30 were invited to participate in this “Building My Image” project. Patients attended a 45-minute, twice weekly group sessions on the benefits of diet and exercise and three times a week in structured physical activities. Monthly BMI and participation were monitored.
Incentives in the form of token gifts were used as rewards for reaching modest goals. The average BMI reduced from 45.3 to 42.6 for the group (47%) that completed the entire study. This group’s average length of stay was 93 days. 80% had schizophrenia diagnosis. The total weight loss for the group was 324 lbs at an average rate of 45.5 lbs per month. Attendance at group sessions ranged from 80% to 91% and for fitness activity from 69% to 85%. This is a simple cost effective model easily incorporated in inpatient long-term care setting.

References:

NR503 Tuesday, May 4, 3:00 p.m.-5:00 p.m.
Switching From Donepezil to Rivastigmine Is Well-Tolerated: Final Analysis
Supported by Novartis Pharmaceuticals Corporation
Leone Atkinson, M.D., USCDMA CNS, Novartis Pharma Corporation, One Health Plaza, East Hanover, NJ 07938;
Jennifer Steadman, M.S.W., Barbara Kounaras, Michael Chen, Ph.D., Danio F. Misrki, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to make medical decisions in the treatment of AD for patients from the assisted living to the nursing home setting, falling on their current therapy for AD.

Summary:
Introduction: Transitioning patients between cholinesterase inhibitors (ChEI) was thought to require a washout period to avoid cholinergic toxicity; however, evidence suggests that abrupt discontinuation of one ChEI, donepezil, may lead to cognitive decline. We evaluated the safety and tolerability of an immediate switch from donepezil to rivastigmine.

Methods: This is an analysis of the safety and tolerability data from the first 28 days of an open-label, multicenter, prospective trial, in which patients were administered rivastigmine 1.5 mg bid within 24 to 36 hours of donepezil discontinuation. Results are compared with adverse event rates from a retrospective analysis of a pivotal, placebo-controlled trial examining patients not treated with a ChEI prior to study entry.

Results: Fifty-eight of 61 patients completed the first 28 days, with no suspected drug-related discontinuations during this period. Incidence of overall gastrointestinal adverse events at Day 7 was 8.2%, and at Day 28 was 11.4%. Corresponding rates for rivastigmine-treated patients in the retrospective analysis of the pivotal trial was 3.3% for day 7.

Conclusion: These study results suggest transitioning patients from donepezil to rivastigmine without a washout period is safe and well tolerated.

References:

NR504 Tuesday, May 4, 3:00 p.m.-5:00 p.m.
BuChE Inhibition as Experimental Alzheimer’s Disease Therapy
Supported by Novartis Pharmaceuticals Corporation
Nigel Greig, Ph.D., Drug Design, National Institute on Aging, 5600 Nathan Shock Drive, Baltimore, MD 21224-6825;
Debomoy Lahiri, Mark Mattson, Jace K. Mamczart, Arnold Brossi, Tadanobu Utsuki, Donald Ingramt, Yue Wang, Giancarlo Pepeuq, Kumar Sambamurti, Carla Scalia, Jack Rogersy, Qian-Sheng Yu, Harold Holloway

Educational Objectives:
At the conclusion of this session, the participant should be able to demonstrate a clear understanding of the role of butyrylcholinesterase in the normal and Alzheimer brain and the value of its inhibition as a new treatment strategy to not only impact cognition but potentially slow disease progression.

Summary:
Introduction: Potent and selective inhibitors of the enzyme butyrylcholinesterase (BuChE), cymserine ((-)4'-isopropylphenylcarbamoylseroleline) analogues, were synthesized to elucidate the central nervous system role of the enzyme. Butyrylcholinesterase, like acetylcholinesterase (ACHE), catalyses the neurotransmitter acetylcholine (Ach) to terminate its action.

Methods/Results: Administered to rats, cymserine analogues readily entered brain, caused long-term selective inhibition of brain BuChE and elevated extracellular ACh levels without affects on AChE. Selective BuChE inhibition augmented LTP in rat brain slices and improved the cognitive performance of 26-month-old rats in a 14-unit T-maze paradigm. Administered to human SH-SY5Y neuroblastsoma cells in culture, cymserine analogues reduced secreted and cellular β-amylloid precursor protein (APP) as well as secreted β-amylloid peptide (Aβ) levels, as determined by Western Blot and ELISA assay, respectively, without effecting cell viability. In accord with cell culture studies, transgenic mice over expressing human APP administered a cymserine analogue daily for three weeks possessed lower Aβ brain levels than vehicle controls.

Conclusions: These studies suggest that selective, reversible, brain BuChE inhibition by cymserine analogues holds potential for the treatment of AD; offering actions on memory as well as intervention at the level of APP and Aβ synthesis.

References:

NR505 Tuesday, May 4, 3:00 p.m.-5:00 p.m.
Viewing Aggressive Television in Childhood: Association With Aggression in Adulthood
Emil F. Coccaro, M.D., Department of Psychiatry, University of Chicago, 5841 South Maryland Avenue, MC#3077, Chicago, IL 60637

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize that viewing aggressive TV programs in childhood is related to impulsive aggression in later in adulthood.
Summary:

Objective: To determine, in adults, the relationship between impulsive aggression and history of viewing and/or identifying with aggressive television characters in childhood.

Methods: 1,327 adult singletons (25–45 years) from the PENNT-wins Study Program completed questionnaires regarding impulsivity, aggression, and regarding how often, in childhood (ages 6–12 years) they watched television shows with aggressive characters and how much they identified with these types of characters. Impulsivity and aggression were assessed by the Barratt Impulsivity (BIS), Life History of Impulsive Behavior (LHIB), Buss-Perry Aggression (BPA), and Life History of Aggression (LHA), scales.

Results: A composite “Aggressive TV” Z-Score correlated directly with each of the impulsivity/aggression measures (range: .12 to .20, all p's < .001). Multiple regression analysis (including age, gender, race, family of origin SES, and possible psychiatric disorder in the model) using a composite “Impulsive Aggression” Z-Score, did not affect this relationship (part r = .18, p < .001).

Conclusions: These results are consistent with those reported recently by Huesman et al., 2003 that demonstrated that the watching and identification of aggressive television characters in childhood is associated with aggression beyond childhood. This factor may be more robust than previously thought.

Funding Source(s): Funded by NIMH: RO1MH63262

References:

NR507
Tuesday, May 4, 3:00 p.m.-5:00 p.m.
The Effect of Bupropion Sustained Release on Weight Loss in Obese Adolescents Supported by GlaxoSmithKline

James W. Anderson, M.D., Endocrinology Department, University of Kentucky, 1030 South Broadway, Suite 5, Lexington, KY 40504-2881; Frank L. Greenway, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to evaluate the use of bupropion SR for overweight adolescents.

Summary:
Introduction: Adjunctive pharmacotherapy may be considered for obese adolescents who are unable to successfully lose weight. Because several studies have demonstrated that bupropion SR is effective in enhancing weight loss in obese adults, this trial assessed the efficacy and safety for obese teens.

Method: Healthy obese subjects aged 13–18 years were randomized in a double-blind manner to bupropion SR or placebo. They were instructed in a hypocaloric balanced diet including two meal replacements (MR, Slim-Fast®) daily. Subjects being treated with bupropion SR were titrated to 150 mg bid for four weeks and then 200 mg bid for 12 weeks. Visits occurred 2, 4, 6, 8, 12, and 16 weeks after randomization.

Results: Subjects were randomized to placebo (n=32) or bupropion SR (n=33) at 2 sites (n=31 and 34). Bupropion SR subjects lost significantly (P<0.01) more weight (kg and % decrease) at 8, 12, and 16 weeks with intention-to-treat and completer analyses than with placebo. At 16 weeks weight loss (% decrease) was: placebo, 2.6% ± 0.9 (SE, n=23); and bupropion SR, 4.9% ± 1.1 (n=26, P=0.0016).

Conclusions: With no significant difference in adverse events, bupropion SR was associated with significantly more weight-loss in obese teens than placebo.

Funding Source(s): Investigator initiated study funded GlaxoSmithKline

References:
Results in Schizophrenia Efficacy of Olanzapine Versus Risperidone: One-Year Results

Objective: To evaluate the efficacy of olanzapine (Olz) compared with risperidone (Ris) after 1 year of treatment.

Methods: This was a multi-center, randomized, open-label, parallel, dose-flexible, one-year study of outpatients with schizophrenia with prominent negative symptoms (SANS Global score > 10). Patients were randomly assigned to treatment with an initial dose of at least 10 mg/day of Olz (n=120) or at least 3 mg/day of Ris (n=115). Improvement in psychopathology was assessed with the SANS Global subscale (primary efficacy measure) and the SAPS and CGI-S scales (secondary efficacy measures). The response rate was defined as a 30% improvement in the SANS Global score.

Results: The mean±SD dose was 12.2±5.8 mg/day for Olz and 4.9±2.0 mg/day for Ris. At year 1, Olz patients showed significantly higher improvement than Ris patients in the SANS Global (p=.015), the SAPS Global (p=.021), and CGI-S (p=.008) scores. The response rate was greater (p=.001) in the Olz group (69.2%) than the Ris group (48.7%).

Conclusions: In outpatients with schizophrenia with prominent negative symptoms, long-term treatment with Olz was associated with significantly better improvement in psychopathology compared with Ris treatment.

Funding Source(s): Supported by funding from Eli Lilly & Company

References:

NR510 Tuesday, May 4, 3:00 p.m.-5:00 p.m.
Is Cognitive Improvement With Antipsychotic Treatment Pseudospecific?
Supported by Eli Lilly and Company
Eva Marquez, M.S., Lilly Research, Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285; Richard S.E. Keefe, Ph.D., Scott E. Purdon, M.D., Stephanie Rock, Karla Alaka, M.S., Saeed Ahmed, M.D., Richard C. Mohs, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to understand the lack of relationship between cognitive improvement and positive and negative symptom improvement following olanzapine pharmacotherapy.

Summary:
Objective: It is hypothesized that olanzapine (OLZ) treatment improves cognitive deficits in schizophrenia and the relationship between these improvements are independent from other symptoms.

Method: Using post-hoc path analyses, we investigated the relationship between cognition, derived from a cognitive battery composite score, and PANSS negative, positive scores, and EPS. Three double-blind, randomized OLZ versus haloperidol studies were included, resulting in a heterogeneous overall sample including first-episode, early-phase, and stabilized chronic schizophrenia patients.

Results: In the first-episode study, at 24 weeks there was a cognitive effect size of 0.48, with the direct therapy effect account-
The high degree of psychosocial impairment imposed by refractory major depression (MD-R) has led clinicians to search for an ever increasing array of effective treatment strategies. The Objectives: of this study were to assess (1) the effectiveness of the sequential administration of cognitive behavior therapy (CBT) to pharmacotherapy non responders and (2) the usefulness of adjunctive quetiapine treatment on the effectiveness of CBT in MD-R.

Methods: 30 patients with at least two eight week treatments with two different classes of antidepressants at maximal dosages were screened. Patients underwent an open three week lithium (Li) augmentation phase. Nonresponders were withdrawn from all antidepressant medication and randomized to either [CBT (12 weekly sessions) + placebo] or, [CBT + quetiapine 25 mg/day titrated up to tolerance or a maximum of 400 mg/day, within 2 weeks]. Pi-rated (HAM-D, MADRS) and self-rated (Hospital Anxiety and Depression Scale) scales were used for efficacy ratings.

Results: 17% of patients were Li responders (40% HAMD score reduction) whereas 13% of patients were open phase drop outs. 22 patients were randomized, 11 in each group. CBT significantly improved all efficacy variables at endpoint (end of study or LOCF) by up to 25%. However, the [CBT + quetiapine] group showed significant improvement in all rating scale scores whereas the [CBT + placebo] group did not (Paired Student’s t-test). Odds Ratio analysis of study completion significantly favored quetiapine adjuvant treatment (Pearson Chi-square).

Conclusion: Li augmentation and CBT were useful clinical strategies in MD-R, albeit with an efficacy lower than that described for patients with less extensive prior pharmacological treatments. Quetiapine was found to be a useful clinical adjunct, appearing to act by helping patients focus on the CBT protocol.

Funding Source(s): This work was supported in part by a grant from AstraZeneca Canada, Inc.

References:

NR512 Tuesday, May 4, 3:00 p.m.-5:00 p.m.
Moclobemide and/or Cognitive-Behavior Therapy in the Treatment of Social Phobia
Jan Prasko, M.D., Ustavni 91, Prague 8 18103, Czechoslovakia

Summary:
The six month study compares the efficacy of three different therapeutic programs for patients with social phobia. Sixty patients were randomly allocated into three groups. The first group was treated with moclobemide and supportive guidance, the second one with group CBT and placebo pills, and the third one with combination of CBT and moclobemide.

Patients were regularly assessed in one month intervals, by an independent reviewer using the Clinical Global Impression Scale (CGI) and Liebowitz's Scale for Social Phobia (LSAS).

Results: Fifty four (23 males and 31 females) completed the six month period of the study. Six patients dropped out during the study. All therapeutic groups showed significant improvement in their CGI and LSAS scores. The improvement was significantly higher in the groups treated with CBT (alone or in combination with moclobemide) in comparison with the group treated with moclobemide alone. There was no significant difference between groups treated with CBT alone and CBT plus moclobemide.

Conclusion: The results indicate that in six months period group CBT is more effective treatment approach in social phobia than moclobemide.

Supported by the research grant CNS LNOOB122 from Ministry of Education, Youth and Sports, the Czech Republic and by the research grants IGA NF/7565-3 and IGA NF/7580-2.

NR513 Tuesday, May 4, 3:00 p.m.-5:00 p.m.
Augmentation of Sertraline With Cognitive-Behavioral Therapy in the Treatment of PTSD
Supported by Pfizer Inc.
Barbara O. Rothbaum, Ph.D., Department of Psychiatry, Emory Clinic, Emory University School of Medicine, 1365 Clifton Road, NE, Atlanta, GA 30322, Edna B. Foa, Ph.D., Jonathan R.T. Davidson, M.D., Shawn P. Cahill, Ph.D., Kathryn M. Connor, M.D.

Educational Objectives:
At the conclusion of this session, the participant will become familiar with the response to medication augmented by cognitive behavior therapy for PTSD in this study.

Summary:
Sertraline and prolonged exposure, a form of cognitive-behavior therapy (CBT) are both effective treatments for PTSD. However,
some patients do not respond to medication, many responders continue to experience residual symptoms, and discontinuation has been associated with relapse. The addition of CBT to medication may improve acute treatment outcome, particularly for those with a partial response to medication, and reduce relapse. We describe an augmentation study in which all participants initially underwent 10 weeks of open label treatment with sertraline followed by randomization to five weeks of continued medication alone or continued medication augmented with 10 sessions of twice-weekly CBT. Results revealed significant reductions in PTSD severity during the initial medication phase followed by additional improvement during the extension phase for those receiving CBT augmentation, but not for those on medication alone. This augmentation effect was particularly noticeable for partial responders to the initial treatment with medication. A significant proportion of participants who achieved good-end-state functioning on medication alone lost that designation at a six-month follow-up, compared to no relapse in the CBT augmentation condition. Thus, augmentation with CBT both improved acute outcome and resulted in greater maintenance of treatment gains during follow-up. Funding provided by Pfizer Pharmaceuticals.

Funding source(s): Pfizer Pharmaceuticals.


**NR514** Tuesday, May 4, 3:00 p.m.-5:00 p.m.

**Personality in Patients With Somatization Disorder in Spain**

Javier Garcia-Campayo, M.D., Department of Psychiatry, Miguel Servet Hospital, Isabel La Católica 1, Zaragoza 50009, Spain; Marta Aida Diez, M.D., Rachel Kowal, M.D., Aida Pascual, M.D.

**Educational Objectives:**

At the conclusion of this session, the participant should be able to diagnose personality traits and disorders in somatization disorder patients

**Summary:**

**Background:** Association between personality disorders (PD) and somatization disorder (SD) is frequent. The few research studies on this subject have been developed in English-speaking countries.

**Aim:** To study personality disorders and traits in SD patients in Spain.

**Methods:** Seventy consecutive SD psychiatric outpatients and a control group of 71 patients diagnosed of mood or anxiety disorders were selected. Personality disorders and personality traits were measured with IPDE and MMPI respectively.

**Results:** Axis II comorbidity was 62.9%. The higher odds-ratio PD in SD patients were paranoid, obsessive-compulsive and histrionic. MMPI showed significant differences between SD patients and controls in all scales except mania. Hypochondriasis, paranoid and schizophrenia scales scored in pathological levels. Conversion “V” (high scores in scales Hs and Hy, and low scores in scale D) was not observed in SD patients. There was no MMPI signs of denial of psychological problems associated with physical complaints.

**Conclusions:** These data are comparable to prior research in Britain and USA.

**References:**


**NR515 WITHDRAWN**

**NR516 Tuesday, May 4, 03:00 p.m.–05:00 p.m.**

**Existential Group Psychotherapy Yields Superior Outcome to Cognitive-Behavioral Group Therapy**

Rendueles Villalba, M.D., Psychiatry Department, Rhode Island Hospital, 593 Eddy Street, Providence, RI 02903; Mark B. Elliot, M.D.

**Educational Objectives:**

At the conclusion of this session, the participant should be able to appreciate the differences between cognitive-behavioral group psychotherapy and existential group psychotherapy and consider the interaction between these treatments and interpersonal group psychotherapy.

**Summary:**

**Objective:** The Rhode Island Hospital Adult Psychiatric Partial Hospitalization Program (PHP) has collected prospective naturalistic outcome data. This afforded an opportunity to investigate the differential outcome of two unique group psychotherapy modalities: Cognitive-Behavioral Group Therapy (CBGT) and Existential Group Therapy (EGT).

**Method:** Improvement in self-reported anxiety, depression, and hopelessness, as measured by the Beck Anxiety Inventory (BAI), Beck Depression Inventory (BDI), and the Beck Hopelessness Scale (BHS), respectively, were the target outcome variables. A mirror-image study was conducted, comparing five months of data pre and post PHP’s transition from CBGT and EGT.

**Results:** Patients treated with EGT whose intake scores indicated severe symptoms demonstrated a significantly greater improvement than similar patients treated with CBGT on all measures.

**Conclusion:** Since the transition from CBGT to EGT entailed a change of only 75 minutes of a six-hour treatment day, it is difficult to attribute this considerable effect solely to the differential efficacy of the isolated treatment components in question. We hypothesize that the combination of EGT and interpersonal group therapy yields synergistic efficacy while the combination of CBGT and interpersonal group therapy is a less ideal (perhaps antagonistic) coupling. A concurrent mirror-image analysis employing the therapeutic milieu process measure, The Group-Climate Questionnaire, yielded independent support of the synergy model proposed.

**References:**

NR517 Tuesday, May 4, 3:00 p.m.-5:00 p.m.

Improvement in Global Functioning in Bipolar Patients: Results From an Open-Label Risperidone Study

Supported by Janssen Pharmaceutical and Research Foundation

Marcia Rupnow, Ph.D., Department of Outcomes Research, Janssen Pharmaceutical Products, L.P., 1125 Trenton Harborton Road, Titusville, NJ 08560, Carla M. Canuso, M.D., Philip G. Janicak, M.D.

Educational Objectives:

- At the conclusion of this session, the participant should be able to: (1) understand the relationship between the Global Assessment Scale score and overall functioning in patients with bipolar disorder; and (2) understand how risperidone treatment affects functioning in patients with bipolar disorder.

Summary:

Objective: To examine the effect of risperidone monotherapy on global functioning in patients with bipolar I disorder.

Methods: A nine-week, open-label(OL) extension trial of risperidone was conducted in patients previously randomized to three weeks of either placebo or risperidone monotherapy for the treatment of acute mania. The Global Assessment Scale (GAS) was used to assess overall functioning. Changes from OL baseline were analyzed using paired t test.

Results: This study included 105 patients who were previously randomized to placebo(RIS/RIS), and 134 to risperidone(RIS/RIS). Mean age was 35.2, and mean modal dose of risperidone was 4.6mg. Mean(SD) OL baseline GAS score was 56.1(17.6) for PLARIS patients, and 66.9(13.0) for RIS/RIS patients. At OL endpoint, mean(SD) scores improved to 66.8(21.7) and 77.7(14.7), an improvement of 10.6 and 10.8 points, respectively (P<.001 in both). Median scores at OL endpoint were 70.0 and 80.0, respectively. Relative to double-blind baseline, the RIS/RIS group improved by 41.9 points, and the PLARIS group by 31.1 points.

Conclusions: Treatment with risperidone resulted in significant and clinically meaningful improvements in overall functioning. Those who received risperidone for the entire 12 weeks improved to a level of minimal or no impairment, while those initially on placebo or risperidone monotherapy for the treatment of acute mania. The Global Assessment Scale (GAS) was used to assess overall functioning. Changes from OL baseline were analyzed using paired t test.

Funding Source(s): Supported by Janssen Pharmaceutical Products, L.P.

References:


NR518 Tuesday, May 4, 2004, 3:00 p.m.-5:00 p.m.

Concurrent Psychotropic and Atypical Antipsychotic Use in Pediatric Inpatients

Supported by Janssen Pharmaceutical and Research Foundation

Eric A. Youngstrom, Ph.D., Department of Psychology, Case Western Reserve, 10900 Euclid Avenue, Cleveland, OH 44106; Robert L. Finding, M.D., Gahan J. Pandina, Ph.D., Scott Flanders, Ph.D., Sarah Jensik, M.S., Marcia Rupnow, Ph.D., Gabrielle Carlson, M.D.

Educational Objectives:

- At the conclusion of this session, the participant should be able to understand how atypical antipsychotic treatment affects BPRS-C scores in pediatric inpatients and describe LOS differences for pediatric inpatients treated with risperidone, quetiapine, and olanzapine.

Summary:

Objective: To compare changes in the Brief Psychiatric Rating Scale for Children (BPRS-C) and length of stay (LOS) in patients...
prescribed an atypical antipsychotics (AA) to those not prescribed an antipsychotic at discharge.

Methods: Descriptive statistics and ANOVA were used to compare differences between and within the group of patients that was prescribed an AA (risperidone, olanzapine or quetiapine) (n=1,131) and the group that had not been prescribed AA at discharge (n=1,741).

Results: The AA treatment group showed greater difficulty at admission with respect to BPRS-C overall score, but at discharge, patients given AA showed greater improvement in BPRS-C behavior problems, thinking disturbances, and psychomotor excitation subscores (P<0.05), but less improvement in depression subscore from admission to discharge than patients given no antipsychotic (P<0.05). AA patients treated with risperidone had shorter LOS than those treated with quetiapine or olanzapine (P<.001).

Conclusions: Patients receiving AA had more significant emotional and behavioral disorders at admission than patients not given AA. The AA treatment group showed greater improvement in behavior problems, thinking disturbances, and psychomotor excitation outcomes than patients given no antipsychotic, but less improvement in depressive symptoms. Among AA treated patients, LOS was significantly shorter for patients treated with risperidone.

Funding Source(s): Janssen Pharmaceutica Products, L.P.

References:

NR520
Tuesday, May 4, 3:00 p.m.-5:00 p.m.
Rivastigmine Is a Potent Inhibitor of Cholinesterase in Plaques and Tangles
Supported by Novartis Pharmaceuticals Corporation
Chandiz Geula, Ph.D., Neuroscience Department, Beth Israel Deaconess, 330 Brookline Avenue, Boston, MA 02215; Mariam Eskander, Nicholas Nalykery, B.S., Leone Atkinson, M.D., Elaine Leung, B.S.

Educational Objectives:
At the conclusion of this session, the participant should be able to:
1. Recognize the ability of rivastigmine to inhibit acetylcholinesterase and butyrylcholinesterase in plaques and tangles in Alzheimer’s disease and understand the possibility of disease alteration through such inhibition.

Summary:
Introduction: Evidence indicates that enzymatically altered acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE) activities are present in plaques and tangles, the pathological hallmarks of Alzheimer’s disease (AD). This study investigated the ability of rivastigmine to inhibit AChE and BuChE activities in plaques and tangles.

Methods: Histochemical methods were used to visualize AChE and BuChE in neurons, axons, glia, plaques and tangles in eight AD brains. Rivastigmine was added to the medium at 10^-9 to 10^-3 M. The potency of rivastigmine was compared quantitatively with AChE inhibitor BW284C51 and BuChE inhibitors iso-OMPA and ethopropazine.

Results: Abundant AChE and BuChE activities were present within plaques and tangles. More plaques contained BuChE than AChE. Rivastigmine was as potent as BW284C51 in inhibiting AChE in plaques and tangles. However, it was more potent in inhibiting BuChE in plaques and tangles than iso-OMPA and was equipotent when compared with ethopropazine.

Conclusion: Rivastigmine results in dose-dependent inhibition of AChE and BuChE in normal neural constituents, plaques and tangles. While rivastigmine inhibits AChE activity, it is a more potent inhibitor of BuChE activity. Administration of rivastigmine is likely to inhibit cholinesterases in plaques and tangles and may interfere with the disease process.

Supported in part by Novartis Pharmaceuticals, Inc.

References:

NR521
Tuesday, May 4, 3:00 p.m.-5:00 p.m.
Treatment of PTSD: A Comparison of Venlafaxine Extended Release, Sertraline, and Placebo
Supported by Wyeth Pharmaceuticals
Jonathan R.T. Davidson, M.D., Department of Psychiatry, Duke University, Trent Drive, 4th Floor, Rm 4082B, PO Box 3812, Durham, NC 27710; Alan Lipschitz, M.D., Jeff Musgnung

Educational Objectives:
At the conclusion of this session, the participant should be able to: (1) compare the efficacy of venlafaxine XR to sertraline and placebo; (2) understand the importance of core components of posttraumatic stress disorder (symptoms of intrusion, avoidance and arousal) in the evaluation of treatment effectiveness.

Summary:
Objective: To compare the efficacy of venlafaxine XR and sertraline in reducing symptoms of moderate-to-marked posttraumatic stress disorder (PTSD).

Methods: Adult outpatients (n=537) with a primary diagnosis of DSM-IV PTSD were randomized to treatment with placebo, venlafaxine XR (37.5–300 mg/day) or sertraline (25–200 mg/day) for 12 weeks. The primary efficacy measure was the change from baseline to endpoint in the CAPS-SX_{17} score. Secondary assessments included remission rate (CAPS-SX_{17} ≤ 20); symptom-free days, and changes from baseline to endpoint in CAPS-SX_{17} symptom cluster scores.

Results: Mean baseline-to-endpoint changes in CAPS-SX_{17} scores were -41.8, -39.4, and -33.9 for venlafaxine XR (P<0.05 vs placebo), sertraline, and placebo, respectively. Changes for venlafaxine XR, sertraline, and placebo in CAPS-SX_{17} cluster scores were -13.0, -11.7, and -11.0 for re-experiencing; -17.1, -16.8, and -13.7 (P<0.05 both active treatments vs placebo) for avoidance/numbing; and -11.8, -10.9, and -9.2 (P<0.05 venlafaxine vs placebo) for hyperarousal. Week 12 remission rates were venlafaxine XR 30.2% (P<0.05 vs placebo), sertraline 24.3%, and placebo 19.6%. Venlafaxine XR was superior to placebo at week 12 for symptom-free days (P<0.05). Mean maximum daily doses were 225 mg venlafaxine XR and 151 mg sertraline.

Conclusion: Venlafaxine XR is effective in the short-term treatment of patients with PTSD.

Funding Source: Wyeth Research

References:
2. Davidson JR, Rothbaum BO, van der Kolk BA, Sikes CR, Farfel GM. Multicenter, double-blind comparison of sertraline and
NR522  Tuesday, May 4, 3:00 p.m.-5:00 p.m.
Escitalopram in the Long-Term Treatment of GAD
Supported by Forest Laboratories, Inc.
Jonathan R.T. Davidson, M.D., Department of Psychiatry, Duke University, Trent Drive, 4th Floor, Rm 4082B, PO Box 3812, Durham, NC 27710; Anjana Bose, Ph.D., Qin Wang, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize that escitalopram 10–20 mg/day is safe and effective in long-term treatment of GAD.

Summary:
Background: Three eight-week, double-blind, placebo-controlled trials of escitalopram have been completed in patients with generalized anxiety disorder (GAD). All three trials have shown that escitalopram is effective and well tolerated in the treatment of GAD.

Objective: Patients completing any of the eight-week trials were given the option of entering an open-label, flexible-dose trial to evaluate the long-term efficacy and tolerability of escitalopram in the treatment of GAD.

Methods: This was a 24-week, open-label, flexible-dose trial of escitalopram 10–20 mg/day. Efficacy assessments included HAMA, Clinical Global Impressions (CGI), and Quality of Life (QOL) scales. Response was defined as a CGI-improvement score of 1 or 2.

Results: A total of 526 patients entered this open-label study. Of these, 299 (57%) completed 24 weeks of treatment. The mean HAMA score at baseline was 13.1. Long-term escitalopram treatment led to continuing improvement in all anxiety and QOL scores. Mean HAMA scores at week 24 for all study completers was 6.9, and 92% of completers were responders. Insufficient therapeutic response led to withdrawal of 4.2% of patients. No tolerability concerns were associated with long-term escitalopram treatment. Treatment-emergent adverse events in the present study were similar in type and frequency to those observed in the acute GAD trials. Adverse events led to withdrawal of 9.9% of patients.

Conclusion: These results support the long-term tolerability and effectiveness of escitalopram in the treatment of GAD.

Funding Source(s): Forest Laboratories, Inc.

References:

NR524  WITHDRAWN

NR525  Tuesday, May 4, 3:00 p.m.-5:00 p.m.
Patient Attitudes Towards a Surgically Implantable, Long-Term Delivery System of Psychiatric Medicine
Steven J. Siegel, M.D., Department of Psychiatry, University of Pennsylvania, 415 Curie Boulevard, Room 145A, Philadelphia, PA 19104; Raquel E. Gur, M.D., Ruben C. Gur, John D. Ragland, Farzin Irani, M.S., Mary Dankert, B.S., Colleen Bresninger, Warren Bilker, Ph.D., Sudha Nair, M.D., Christian Kohler, M.D., Stephen J. Kanes, M.D., Bruce I. Turetsky, M.D., Paul J. Moberg, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to learn about psychiatric patients’ attitudes and beliefs toward illness, medication and surgical implants.

Summary:
Objectives: The introduction of surgically-implantable medication delivery systems provides psychiatric patients with reversible, uninterrupted access to medication for up to 14 months. We designed and administered a survey to assess patients’ attitudes and beliefs toward illness, medication, and this new treatment method.

Methods: The survey included questions about demographics, insight, medication adherence, and surgical implants.
Results: The sample of 206 psychiatric patients was almost equally split between favorably and unfavorably considering implants. Patients favorable towards implants ascribed cognitive limitations as reasons for missing doses, recognized the benefits of medication in general and understood that the implant would be inserted under the skin. Favorable consideration of implants was positively correlated with the desire to avoid adverse consequences of missing medication, stay well, avoid the need for daily oral medications and decrease family burden. Unfavorable consideration of implants was related to a preference to take medication orally, concern about feeling controlled, unwillingness to try something new and not understanding that the implant would be placed under the skin.

Conclusions: The results indicate that most patients recognize the difficulties of medication adherence and the need for better methods to attain therapeutic response. Thus, the study provides impetus for future work in this area.

Funding Source(s): Stanley Medical Research Institute

References:


NR526 Tuesday, May 4, 3:00 p.m.-5:00 p.m.
The Impact of Crisis Intervention on Emergency Psychiatric Admissions in Patients With Depressive Disorders

Cristian Damasa, M.D., Emergency Department, University Hospital, Rue Micheli-du-Crest 24, Geneva 1211, Switzerland; Vedat Sar, M.D., Laurence Borras, M.D., Lionel Cailnoi, Thierry di Clemente, Antonio Andreoli, Charles Pull

Educational Objectives:

At the conclusion of this session, the participant should be able to choose the most appropriate critical care for depressive patients.

Summary:

Objective: The aim of this study was to investigate the impact of crisis intervention on psychiatric emergency admissions in patients with depressive disorders (criteria DSM IV).

Method: All subjects with depressive disorders admitted to the psychiatric emergency unit of a general hospital in two seven-month study periods before (355 patients) and after (431 patients) the introduction of a crisis intervention program were considered for participation.

Results: A comparison between the two periods demonstrated a significant decrease in the number of voluntary hospitalizations whereas the number of patients with more than five subsequent outpatient consultations increased significantly. There was no decrease of hospitalizations among patients who had major depressive disorder with psychotic symptoms. The highest decrease in the hospitalization rate was among patients diagnosed as having a dissociative disorder or borderline personality disorder. Crisis intervention was more effective on female patients.

Conclusions: These preliminary findings suggest that the presence of a crisis intervention program leads to a shift from hospitalization to outpatient psychotherapeutic management among emergency psychiatric admissions, particularly for patients with a personality disorder.

References:


NR527 Tuesday, May 4, 3:00 p.m.-5:00 p.m.
Ziprasidone Long-Term Post-Switch Efficacy in Schizophrenia
Supported by Pfizer Inc.

George M. Simpson, M.D., Department of Psychiatry, University of Southern California, 2020 Zonal Avenue, IRD Room 20, Los Angeles, CA 90033; Mohamed H. Fayek, M.D., Peter J. Weiden, M.D., Stephen R. Murray, M.D., Judith Dunn, Ph.D., Lewis Warrington, Ph.D., Antony D. Loebel, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should have a better understanding of the long-term efficacy and tolerability of ziprasidone in schizophrenic outpatients switched from other antipsychotics because of inadequate therapeutic response or poor tolerability.

Summary:

Objective: To evaluate ziprasidone's long-term efficacy and tolerability in schizophrenic outpatients switched from other antipsychotics.

Methods: Three open-label, flexible-dose continuation studies enrolled completers of 6-week trials initially switched to ziprasidone from conventional, olanzapine, or risperidone. Primary efficacy variables were changes to endpoint from core baseline in PANSS Total and CGI-S, with analysis by paired t tests in ITT (LOCF) and completer populations.

Results: Overall median treatment duration was 215 days (range 7–824 days); median dosage at penultimate treatment day was 120 mg/d. In those switched from conventional, mean PANSS Total score improved significantly in ITT patients (n=7–6.3 [P<0.01]) and in completers (n=30; –10.1 [P<0.01]); CGI-S improved significantly in both (–0.4 [P<0.001] and –0.7 [P<0.0001], respectively). In patients switched from olanzapine (n=71), completers (n=25) exhibited significant improvements in PANSS Total (–10.0 [P<0.01]) and CGI-S (–0.4 [P<0.05]). In patients switched from risperidone (n=43) completers (n=17) exhibited significant improvements in PANSS Total (–10.9 [P<0.05]) and CGI-S (–0.9 [P<0.001]). Ziprasidone was well tolerated, with insomnia alone having an incidence >10% in all three groups. No patient had QTc interval ≥500 msec.

Conclusions: Patients switched to ziprasidone demonstrated long-term improvement in symptoms and illness severity. Ziprasidone was well tolerated.

Funding Source(s): Supported by Pfizer

References:


Consequences of Nonremitted Depression in Health Care Utilization and Productivity: A 23-Year Follow-Up

Supported by Eli Lilly and Company

Suzanne Graden, Ph.D., Outcomes Research, Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285; Ruth Cronkite, Ph.D., Donna Roybal, B.A., Jacob Robson, B.A., Genery Booster, B.A., Rebecca Robinson, M.S., Ralph W. Swindle, M.D.

Educational Objectives:

At the conclusion of this session, participant should be able to demonstrate how the self-reported burden of illness (direct and indirect costs) of depression is impacted by the remission status 23 years post-diagnosis for major depression.

Summary:

Objective: Assess the association between remission status on health care utilization and productivity loss of a 23-year cohort in patients diagnosed with major depression.

Methods: A cohort of 424 patients treated for unipolar depression in 1980 was followed longitudinally. After 23 years, a response rate of 72.9% of the surviving cohort participated. DSM-IV depression criteria were used to establish remission status for this analysis.

Results: The self-reported physician visits was higher for currently depressed vs. currently remitted respondents (9.0/year vs. 4.5/year, p-value = .007). The currently depressed utilized more antidepressants than the currently remitted (1.9 vs. 1.0, p-value <.001). The reduced activity days due to physical or emotional problems (8.5/30-day vs. 2.4/30-day) and days kept in bed by physical or emotional problems (4.1/30-day vs. 8.3/30-day) were higher for currently depressed vs. currently remitted (p-value <.001).

Conclusion: When controlling for the socio-demographic characteristics of age, sex, and education, self-reported health care utilization and losses in productivity are higher in currently depressed patients than currently remitted depressed patients. Despite treatment, 34% of the surviving cohort failed to achieve remission of symptoms and depression continues to negatively impact their work productivity, ability to function socially and result in increased overall health care utilization.

Funding Source(s): Eli Lilly and Company

References:


Objective: The utility of lithium in the prophylaxis of bipolar illness has been well established. However, lithium has many burdensome side effects including the long-term problem of renal toxicity. Over the last decade, anticonvulsants have been utilized in the acute and long-term treatment of bipolar illness as an alternative to lithium. It is the purpose of this study to examine the prophylactic efficacy of depakote & carbamazepine for bipolar disorders in a naturalistic clinical setting.

Method: To date we have followed 54 patients on depakote and 43 patients on carbamazepine who after six months stability of mood were then followed until one of three outcomes-termination well (all patients continuously well until Aug 31, 1998 the endpoint of this preliminary analysis), dropout or relapse being defined as having a breakthrough manic or depressive episode as defined by DSM-IV, requiring either hospitalization or additional or other pharmacotherapy.

Results: Overall 28/54 patients on depakote (51.9%) and 19/43 on carbamazepine (44.2%) suffered a known affective relapse over a subsequent 4 year course. The rates of relapse for manic or depressive relapse was equal for either agent. More patients dropped out on carbamazepine-13/43 (30.2%) vs 7/54 on depakote (13.0%). An attempt to stabilize 20 of the patients who failed on either mood stabilizer with a manic episode with lithium + the anticonvulsant (depakote or carbamazepine) led to better prophylactic effect for the combination

Conclusion: Both depakote & carbamazepine had comparable efficacy in the long-term treatment of bipolar illness. Comparisons between the naturalistic studies in the literature and double-blind studies will be discussed as well as possible reasons for these differences.

There was no funding for this study.

References:


Rapid Relief of Psychotic Symptoms With Bilateral ECT: A Report From the CORE Trial

Charles H. Kellner, M.D., Department of Psychiatry, UMDNJ New Jersey Medical School, 183 South Orange Avenue, Suite F1439, Newark, NJ 07103; Rebecca G. Knapp, Ph.D., Georgios Petrides, M.D., Mustafa M. Husain, M.D., Keith G. Rasmussen, M.D., Teresa A. Rummans, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to describe the time course of relief of psychotic symptoms in psychotic depression with ECT

Summary:

Introduction: Patients with psychotic depression represent an important subset of those referred for ECT. As part of an ongoing NIMH-funded, randomized multi-center trial, we evaluated the rapidity of a course of ECT in relieving psychotic symptoms.

Methods: As of 2003, 444 patients had received a course of bilateral ECT. HAM-D24 ratings were obtained at baseline and after each ECT (3x/week). HAM-D24 items 2 (guilt feelings and delusions), 15 (hypochondriasis), 16 (loss of insight), and 20 (paranoid symptoms) were used to provide a psychosis severity measure. Patients meeting SCID IV criteria for psychosis and who

Anticonvulsant Prophylaxis in Bipolar Illness

Eric D. Peselow, M.D., Department of Psychiatry, New York University School of Medicine, 32 Bassett Avenue, Brooklyn, NY 11234; Mary Anne Pressman, M.D., Ronald R. Fieve, M.D.

Educational Objectives:

The educational objective is to evaluate the prophylactic efficacy of carbamazepine and depakote in a naturalistic clinic setting

Objective: While patients with bipolar disorder (BD) often have superimposed affective episodes, there is little information on the relative efficacy of treatment-resistant BD patients with and without melancholic symptoms. This study will examine the efficacy of carbamazepine and depakote in a naturalistic clinic setting.

Methods: A cohort of 424 patients treated for unipolar depression in 1980 was followed longitudinally. After 23 years, a response rate of 72.9% of the surviving cohort participated. DSM-IV depression criteria were used to establish remission status for this analysis.

Results: The self-reported physician visits was higher for currently depressed vs. currently remitted respondents (9.0/year vs. 4.5/year, p-value = .007). The currently depressed utilized more antidepressants than the currently remitted (1.9 vs. 1.0, p-value <.001). The reduced activity days due to physical or emotional problems (8.5/30-day vs. 2.4/30-day) and days kept in bed by physical or emotional problems (4.1/30-day vs. 8.3/30-day) were higher for currently depressed vs. currently remitted (p-value <.001).

Conclusion: When controlling for the socio-demographic characteristics of age, sex, and education, self-reported health care utilization and losses in productivity are higher in currently depressed patients than currently remitted depressed patients. Despite treatment, 34% of the surviving cohort failed to achieve remission of symptoms and depression continues to negatively impact their work productivity, ability to function socially and result in increased overall health care utilization.

Funding Source(s): Eli Lilly and Company

References:


had scores of ≥2 on any of the HAM-D psychosis items at baseline (n=119) were followed for resolution of psychosis severity (≤ on all psychosis items).

Results: Approximately 45.4% (54/119) had all psychosis items resolved after 3 ECT (1 week); 68.1% (81/119) resolved after six ECT (2 weeks); only 22% failed to resolve over the ECT course. The psychosis severity score (sum of psychosis items) decreased from baseline on average 60% (+37%) after 3 ECT; the HAM-D total score declined on average 48% after three ECT.

Conclusion: These data demonstrate that ECT has a rapid beneficial effect on the psychotic symptoms of psychotic depression.

Funding Source(s): NIMH grant #MH55495

References:

NR531 Tuesday, May 4, 3:00 p.m.-5:00 p.m.
Long-Term Cognitive Improvement: Ziprasidone Versus Olanzapine
Supported by Pfizer Inc.

Philip D. Harvey, Ph.D., Department of Psychiatry, Mt. Sinai Medical Center, 1425 Madison Avenue, New York, NY 10029; Christopher Bowie, Ph.D., Anthony D. Loebel, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant will have an increased understanding of the cognitive changes associated with long-term treatment with atypical antipsychotic medication.

Summary:
Background: It is unclear whether long-term treatment with atypical antipsychotics yields continued improvement in cognitive function. We compared olanzapine and ziprasidone treatment of cognitive impairments in a double-blind, six-month extension of a six-week randomized, controlled trial.

Methods: Patients entered the 6-week study naïve to both medications and could enter the extension if they had CGI-I ≥2 or ≥20% improvement in PANSS Total during the core study. A cognitive battery measured verbal learning, executive functioning, visuospatial speed, verbal fluency, and vigilance.

Results: In both ziprasidone (n=62) and olanzapine (n=71) groups, substantial cognitive improvements occurred from baseline to endpoint of the extension. Improvements (presented in effect size units) were generally uncorrelated with changes in PANSS or ESRS.

Conclusions: Long-term treatment of patients with early response to ziprasidone or olanzapine is associated with incremental cognitive gains that are at least twice that observed in short-term trials. Thus, cognitive benefits of atypicals may increase over time.

Funding Source(s): Supported by funding from Pfizer Inc.

References:
2. Harvey PD, Siu CO, Romano S: Randomized, controlled, double-blind, multicenter comparison of the cognitive effects of ziprasidone versus olanzapine in acutely ill inpatients with schizophrenia or schizoaffective disorder. Psychopharmacology (Berl). 2003 Nov 13 [Epub ahead of print].

NR532 Tuesday, May 4, 03:00 p.m.—05:00 p.m.
Ziprasidone Versus Olanzapine: Contrasts in Coronary Heart Disease Risk
Supported by Pfizer Inc.

David J. Harrison, Ph.D., Pfizer Incorporated, 235 East 42nd Street, New York, NY 10017; Megan C. Leaderer, M.P.H., Antony D. Loebel, M.D., Stephen R. Murray, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should have greater understanding of the relative potential impact of ziprasidone and olanzapine on coronary heart disease (CHD) risk factors and overall CHD risk in schizophrenic patients.

Summary:
Objective: To examine differences in coronary heart disease (CHD) risk arising from short-term treatment with ziprasidone and olanzapine.

Methods: Hospitalized schizophrenic adults underwent six weeks' randomized, double-blind treatment with ziprasidone or olanzapine, with data collected at baseline and endpoint for fasting lipids and weekly for BP. A Framingham algorithm was used to calculate percentage CHD risk over 10 years in patients ≥30 years (per algorithm). Baseline-to-endpoint LS mean changes in age-adjusted risk by sex were compared using ANCOVA (baseline adjusted).

Results: In men, TC and LDL-C changes were significant for olanzapine (n=56; +22.7 and +13.9 mg/dL, respectively) versus ziprasidone (n=50; −10.0 and −6.9 mg/dL, respectively) (P<0.01 for TC, P<0.05 for LDL-C). CHD risk in men increased by 0.8% (baseline 4.2%) with olanzapine (n=55) and decreased by 0.2% (baseline 4.5%) with ziprasidone (n=46) (P<0.05 between groups). In women, between-group differences were insignificant for lipid changes and CHD risk. Neither treatment had significant effects on BP.

Conclusion: In short-term treatment of men, olanzapine caused significant changes in lipid profile versus ziprasidone, with a consequent significant increase in CHD risk versus ziprasidone. These findings, coupled with those of significant weight gain with olanzapine versus ziprasidone, warrant investigation in longer term trials.

Funding Source(s): Supported by funding from Pfizer Inc.

References:

NR533 Tuesday, May 4, 3:00 p.m.-5:00 p.m.
Normalization of Cognitive Function With Long-Term Ziprasidone or Olanzapine
Supported by Pfizer Inc.

Christopher Bowie, Ph.D., Psychiatry Department, Mt. Sinai, 1425 Madison Avenue, 4th Floor, New York, NY 10029; Philip

References:
2. Harvey PD, Siu CO, Romano S: Randomized, controlled, double-blind, multicenter comparison of the cognitive effects of ziprasidone versus olanzapine in acutely ill inpatients with schizophrenia or schizoaffective disorder. Psychopharmacology (Berl). 2003 Nov 13 [Epub ahead of print].
2. Palmer, BW, et al: Is it possible to be schizophrenic and neuro-
ance. Olanzapine treated subjects showed a similar pattern of
ziprasidone over 6 months was normalization of cognitive perform-
difference in extent of change and likelihood of normalization.
50% were still impaired. There was no significant between group
improvement.

5. Miguel-Hidalgo, Ph.D., Department of Psychiatry,
tiation in rats.

References:
1. Satou T, Cummings BJ, Cotman CW: Immunoreactivity for
Bcl-2 protein within neurons in the Alzheimer’s disease brain
tection by memantine against neurodegeneration induced by
beta-amyloid(1-40). Brain Res. 2002; 958:210-221.

NR534 Tuesday, May 4, 3:00 p.m.-5:00 p.m.
Memantine Prevents AB1-40-Induced Increase in
Hippocampal BCL-2 Expression
Supported by Forest Laboratories, Inc.
Jose J. Miguel-Hidalgo, Ph.D., Department of Psychiatry,
University of Mississippi, 3500 North State Street, Box 127,
Jackson, MS 39216; Ian Paul, Ph.D., Valerie Wanzo, B.S.,
Pradeep Banerjee, Ph.D.

Educational Objectives:
At the conclusion of this session, the participants should be
able to assess the effect of memantine on neurotoxicity and B-
cell leukemia gene (bcl-2) expression following Abeta(1-40)
injection in rats.

Summary:
The protein product of the B-cell leukemia gene (bcl-2) promotes
cell survival. The expression of Bcl-2 protein in the hippocampus
and entorhinal cortex of Alzheimer’s disease brains has been
found to increase with disease severity, suggesting that degenera-
tive processes can trigger the expression of neuroprotective fac-
tors. Therefore, increased expression of Bcl-2 can be used as a
marker of compensatory mechanisms subsequent to neurodegen-
etive sequelae. Injectons of beta amyloid peptides [Abeta(1-
40)] into the rat hippocampus produce lesions in the dentate gyrus
and the CA1 area of the hippocampus. In this model, the uncom-
petitive NMDA receptor antagonist, memantine, reduces the ex-
tent of Abeta(1-40)-induced lesions in the hippocampus.
We first determined whether Bcl-2 immunoreactivity was altered
following bilateral injections of Abeta(1-40) into the rat hippocam-
pus. We also determined the effects of memantine (administered
s.c. via osmotic mini-pump for 9 days) on Bcl-2 expression in
Abeta(1-40)-injected rats.
Injections of Abeta(1-40) resulted in an increase in the number
of Bcl-2 immunoreactive cells at the injection site and occasionally
in surrounding areas, Memantine significantly reduced the size of
Abeta(1-40) lesions and the number of cells immunoreactive for
Bcl-2 in the CA1 area.
These data extend and confirm earlier findings that memantine
provides neuroprotection against Abeta(1-40)- induced neurotoxi-
city.

Funding Source(s): Forest Laboratories, Inc.

References:
1. 1. Satou T, Cummings BJ, Cotman CW: Immunoreactivity for
Bcl-2 protein within neurons in the Alzheimer’s disease brain
tection by memantine against neurodegeneration induced by
beta-amyloid(1-40). Brain Res. 2002; 958:210-221.

NR535 Tuesday, May 4, 3:00 p.m.-5:00 p.m.
No Evidence of Tachyphylaxis With Long-Term Non-
Nightly Use of Zolpidem
Supported by Sanofi-Synthelabo, Inc.
W. Vaughan McCall, M.D., Department of Psychiatry, Wake
Forest University, Medical Center Boulevard, 8th Floor,
Winston-Salem, NC 27157; Michael L. Perlis, Ph.D., Andrew D.
Krystal, M.D., James K. Walsh, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able
to recognize that improvements in sleep parameters gained with
non-nightly administration of zolpidem were stable over the 12-
week study period.

Summary:
Objective: Long-term patient response to non-nightly hypnotic
use is not well described in the literature. The goal of this study
was to evaluate efficacy trends of non-nightly dosing of zolpidem,
over a three month period.
Methods: 199 patients meeting the DSM IV criteria for primary
insomnia were randomized to either zolpidem 10 mg or placebo
taken 3-5 nights/week for 12 weeks, in a multicenter, double-
blind, placebo-controlled clinical trial. Both groups were assessed
for Sleep Latency (SL), Number ofAwakenings (N0A), Wake After
Sleep Onset (WASO), and Total Sleep Time (TST). Group values
were biweekly averages for nights when pill used (+Pill), no pill
used (-Pill), and for all nights (All). Serial ANOVAs analyzed treat-
ment efficacy, with three mixed-model 2 x 7 ANOVAs run for each
condition.
Results: Tachyphylaxis was not evidenced. ANOVAs for zolpi-
dem groups (+Pill, -Pill, All) indicate that clinical gains were not
reduced over time. TST showed a tendency to increase over the
study period. SL showed a tendency to decrease. Clinical gains
for NOA and WASO were stable from weeks 1 and 2 to weeks
11 and 12.
Conclusion: Observed clinical gains obtained with zolpidem did
not diminish over the course of the 12-week study.
Early Symptom Response During Treatment With Duloxetine 60 MG: HAMD17 Items

Robert M.A. Hirschfeld, M.D., Psychiatry & Behavioral Science, University of Texas Medical Branch, 301 University Boulevard 1.302RSH, Galveston, TX 77555-0188; Craig Malinconodi, Ph.D., Jeffrey W. Clemens, Ph.D., Michael J. Delke, M.D.

Educational Objectives:
At the conclusion of this presentation, the participants should be able to interpret various definitions of remission of MDD, and recognize the impact of treatment of all symptom domains, particularly painful physical symptoms on achieving remission.

Summary:
Objectives: A more rapid onset of antidepressant action for patients with major depressive disorder (MDD) may improve pharmacological management and reduce the societal burden, including MDD-associated health care costs. We characterized the time to onset of symptom responses during treatment of MDD patients with duloxetine.

Methods: Data were pooled from 2 acute placebo-controlled trials of duloxetine 60 mg QD (11 weeks), a balanced and potent dual reuptake inhibitor of serotonin and norepinephrine. Analysis of individual HAMD17 items was performed to determine the time to onset of action in response to duloxetine (e.g. Thase et al, 2001). Patients who remit by this definition have been shown to have a lower risk of relapse (Paykel et al., 1995) and improved therapy.

Results: Compared with placebo-treated patients (n=251) at week 1, duloxetine-treated patients (n=244) had improved scores (p<.05) on items 1 (depressed mood), 2 (guilt), 3 (suicidality), 7 (work/activities), and 10 (anxiety). This improvement was maintained for all of these items through 11 weeks. However, placebo-treated patients had lower scores on items 12 (somatic symptoms) and 16 (weight loss) at week 1 (p<.05 vs. duloxetine-treated patients).

Conclusions: Compared with placebo for the treatment of MDD, duloxetine 60 mg QD demonstrated greater improvement on multiple individual HAMD17 items, especially emotional symptoms (depressed mood, guilt, and anxiety) and suicidality. This improvement was observed after only 1 week of duloxetine treatment.

References:
with diabetic neuropathy and be able to identify treatment options for this condition.

**Summary:**

**Background:** Duloxetine, a balanced and potent dual reuptake inhibitor of serotonin and norepinephrine, was found to be safe and effective in the acute treatment of pain associated with diabetic neuropathy (Goldstein et al., 2003). The objective of the study's extension phase was to examine the safety of up to 52-weeks exposure to duloxetine in comparison to routine care, and to compare the effect of these treatments on progression of diabetic complications.

**Methods:** In this 52-week, multicenter, open-label study extension, 337 patients with diabetic neuropathic pain were re-randomized to either duloxetine 60 mg BID or routine care. Diabetic complications were measured using the physical examination portion of the Michigan Neuropathy Screening Examination (MNSI; neuropathy progression) microalbumin/creatinine ratio (nephropathy progression), and ophthalmologic examination with fundus photograph (retinopathy progression). Treatment effects on QOL were compared using the Short Form-36 and EQ-5D version of the EuroQol instrument.

**Results:** There were no significant differences between treatment groups regarding neuropathy, nephropathy or retinopathy progression. Discontinuation rates due to adverse events (AEs) were 9.6% and 14.0% for routine care and duloxetine, respectively. Serious adverse events (SAEs) were reported by 19.1% of routine care patients and 14.4% of duloxetine patients. Duloxetine was not significantly greater than routine care regarding the occurrence of SAEs or AEs. There were no significant differences in the number of hypoglycemic events or treatment-emergent abnormal HbA1c or lipids. Duloxetine was significantly better than routine care on the bodily main subscale of the Short Form 36 Health Survey and the EQ-5D Index.

**Conclusion:** In this study, duloxetine 120 mg/day was safe and well-tolerated in the long-term treatment of diabetic neuropathic pain. Duloxetine was superior to routine care on several measures of quality of life.

**References:**


**NR540**

**Tuesday, May 4, 3:00 p.m.-5:00 p.m.**

**Health Care Costs of Vascular Dementia in Community-Dwelling Patients**

**Supported by Pfizer Inc.**

Howard Fillit, M.D., Institute for the Study of Aging, 767 Fifth Avenue, Suite 4200, New York, NY 10153; Jerrold W. Hill, Ph.D., Robert Futterman, Ph.D., Sonali N. Shah, R.Ph.

**Educational Objectives:**

- At the conclusion of this session, the participant should be able to: (1) understand the potential healthcare costs of vascular dementia in an aging population; (2) identify opportunities for improving healthcare delivery for the benefit of vascular dementia patients and society.

**Summary:**

**Background:** Although 9–23% of U.S. dementia patients are diagnosed with vascular dementia (VaD), little is known about VaD-associated healthcare costs and utilization.

**Objective:** To compare health care costs of VaD, Alzheimer's disease (AD), other dementias (OD), cerebrovascular disease without dementia (CVD), and no dementia or CVD (control).

**Methods:** Subjects were selected from Medicare beneficiaries (enrolled in Medicare+ Choice Plan, 1999–2002). Health care costs were derived from claims and encounter data. Medical care setting costs were identified from place-of-service codes. Contrasts of adjusted costs were derived from regression analyses, controlling for age, gender, coexisting medical conditions, and mortality.

**Results:** 578 VaD, 1722 AD, 957 OD, 2718 CVD, and 14,023 control subjects were identified. Annual health care costs were: $2,708 for VaD, $3,388 for AD, $14,007 for OD, $11,946 for CVD, and $4,010 for controls. Regression-adjusted costs for VaD were $7,680 higher than controls and $4,782 higher than the CVD group (P<0.0001). Adjusted costs for VaD were significantly higher than...
CVD for medical services (e.g., hospital) and significantly lower for physician office visits.

Conclusions: Costs for VaD patients were substantially higher than all comparison groups. Management and treatment of VaD within a physician office visit could reduce costly acute care and improve patient well-being.

Funding Source(s): Pfizer Inc.

References:

NR541 Tuesday, May 4, 3:00 p.m.–5:00 p.m.
Transitional Case Management for Dually Diagnosed Patients
David A. Smelson, Psy.D., MHBS, Van Johnson Health Care System, 151 Knollcroft Road, Building 143, Lyons, NY 07939; Miklos F. Losonczy, M.D., Kathleen Castles-Fonseca, Psy.D., Bradley Sussner, Phyllis Stewart, Maureen Kaune, M.D., Douglas M. Ziedonis, M.D.

Educational Objectives:
At the conclusion of the presentation, clinicians and administrators should better understand effective methods of transitioning people from inpatient to outpatient care.

Summary:
Background/Objective: Individuals with co-occurring mental illness and substance abuse poorly engage in outpatient treatment following discharge from Acute Psychiatry. This difficult transition often results in re-hospitalization. We developed an eight-week community linkage intervention to improve outcomes during this vulnerable period.

Method: Fifty-nine dually diagnosed veterans participated in the study. Twenty-six subjects received the new Transitional Case Management (TLC) and outpatient Mentally Ill Chemical Abuse Treatment (MICA), and 33 were discharged as usual to MICA.

Results: Veterans who received TLC treatment had better attendance at the initial outpatient screening (.02) and the follow-up appointment (.001), more days treated in the outpatient MICA care during the transitional period (.001), and greater pharmacy prescription pick-ups (.11). These subjects were also less likely to be lost to follow-up after six weeks (.0001). Furthermore, six-month post-treatment outcomes showed that the TLC group had a significant reduction in psychiatric re-hospitalization days (.05), higher functioning on the Global Assessment in Functioning scale (.0001), and greater reductions in symptom severity on all the BASIS-32 subscales (.006, .006, .001 and .002).

Conclusion: TLC had robust treatment effects well beyond the eight weeks of treatment and appeared to decrease the recidivism common among this population.

References:

NR542 Tuesday, May 4, 3:00 p.m.–5:00 p.m.
A Review of SSRI Comparison Trials
Mark Zimmerman, M.D., Department of Psychiatry, Rhode Island Hospital, 235 Plain Street, Suite 501, Providence, RI 02905; Michael A. Postemak, M.D., Iwona Chelminski, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to describe the response rates for the different SSRIs and, based on these findings, the sample size requirements for studies comparing two SSRIs.

Summary:
Background: As a class, the selective serotonin reuptake inhibitors (SSRIs) are the most frequently prescribed antidepressant medications. There are now 28 published comparisons of SSRIs. We review this literature in order to estimate response rates to guide researchers in determining appropriate sample sizes for drug-drug comparison studies.

Methods: In summarizing the results of these studies we focused on outcome at endpoint based on intent to treat analyses. Almost all studies used multiple outcome measures. In fact, the data from a single measure was often analyzed in several ways. For example, studies using the Hamilton Rating Scale for Depression (HRS), the most frequently used symptom severity outcome scale, have examined change in total scores, change in HRS factor scores, change in the scores on each of the individual items, percentage of patients whose total score improved by at least 50%, and percentage of patients who scored below a cutoff score at the end of treatment. The number of outcome comparisons in the 28 studies ranged from 1 to 41, with a total of 394 outcome variables examined (mean=14.1).

Results: In 6 (21.4%) studies one SSRI was significantly more effective than another on at least one outcome measure. Across studies, there were significant differences between SSRIs on 11 of the 394 (2.8%) outcome variables, less than what would be expected based on chance alone. We computed the response rates for each medication across studies and found that for each SSRI (except fluvoxamine for which data was available from only a single small study) the responder rate was between 60% and 70% (citalopram—69%; fluoxetine—63%; paroxetine—63%; sertraline—67%). To detect a difference in response rates of 63% vs. 69%, the maximum difference between the medications, with a power of .80 and a two-sided alpha level of .05, approximately 1,000 subjects would be needed in each group.

Conclusion: Studies comparing the SSRIs have been underpowered to find differences between medications. Power analyses should be included and discussed in studies comparing medications.

References:

NR543 Tuesday, May 4, 3:00 p.m.–5:00 p.m.
Characterization of the Polifractured Patient’s Psychological Demand
Wilze L. Bruscato, D.R., Psychology, Santa Casa, Borges Lagoa 1231 Conji 82, Sao Paulo, SP 04030020, Brazil; Marcela M. Kitayama, B.S., Clarissa DeFranco, Fernanda Silva Machado, Fernanda T. Orsati, Giselle M. Pedreira, Diane
Portuigues, Fernando M. Sarnes, Ana P. Silva, Marcia V. Torres

Educational Objectives:
At the conclusion of this session, the participant should be able to acknowledge the importance of psychological attendance to polyfractured patients during hospitalization as well as preventive steps adoption.

Summary:
Introduction: Psychology at the hospital has been an important resource of assistance to patients, their families and care staff. Its importance also includes the assistance to fractured patients victims of trauma who usually are totally healthy people before the trauma and abruptly find themselves hospitalized.

Objective: To characterize the infirmary population at the orthopedics and traumatologia Department from Santa Casa de São Paulo.

Methods: 67 fractured patients, both genders, ages between 18 and 92, fulfilled the Social-Demographics File Card and the Psychological Evaluation Protocol during approximately 50 minutes long interviews at the hospital bed.

Results: Population’s medium age (61.2% males and 38.8% females) was 45.3 years old. 7.6% were white and 42.6% were single people. Only 7.5% accomplished university degree and 40.3% didn’t work. Regarding the diagnosis, 64.2% presented inferior member fracture as the main consequence of traffic accidents (37.3%), from which sample 44.8% referred alcohol consumption. The most frequent emotional reactions in trauma situations present to be rationalization and acceptance (32.7%). The majority refers good social (51.3%), affective (54.2%) and familiar (66.7%) relationships. 75% of the sample presented adaptive psychological resources.

Discussion: The findings indicate necessity of psychological attendance to 25% of this population as well as preventive interventions including group discussion about specific subjects (alcohol, youth, traffic accidents, fallings, elderly age).

References:

NRS44 Tuesday, May 4, 3:00 p.m.-5:00 p.m.
Veterans’ Health and Access to Care in the Year Following 9/11
Laurel Copeland, Ph.D., VA HSR&D, 2215 Fuller Road, 114, Ann Arbor, MI 48105; Carol E. Fletcher, Ph.D., Judith Patterson, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the increased vulnerability of persons with PTSD symptoms when a disaster occurs.

Summary:
Objective: To explore the adequacy of Veterans Affairs’ (VA) response to patient needs after a terrorist attack, this study assessed veterans’ perceptions of their health and healthcare in the year following September 11th, 2001.

Method: A random sample of outpatients seen at a Manhattan (NYC) or Midwestern VA during 9/12/2001-9/30/2002 was mailed a questionnaire (64% response rate). Multivariate regression assessed the effects of site, demographics, military service, and post-traumatic stress disorder (PTSD) on health status, care-seeking, and satisfaction with healthcare among 490 participants.

Results: Veterans from NYC scored higher on perceived health and satisfaction that their providers listened to them. Patients with more PTSD symptoms reported lower global health scores, more symptoms related to 9/11, and less satisfaction with: care received, quality of care, opportunity to explain, and feeling their providers listened. They reported difficulty getting an appointment promptly and were more likely to seek care outside the VA for 9/11-related problems.

Conclusion: Proximity to the 9/11 terrorist attacks had little relationship to patients’ perceptions of their health and healthcare, while symptoms of PTSD had a pervasive effect. VA patients with symptoms of PTSD may benefit from outreach efforts following catastrophic events, regardless of their proximity to the events.

Funding Source(s): VA Health Services Research & Development

References:

NRS45 Tuesday, May 4, 3:00 p.m.-5:00 p.m.
Offsetting Metabolic Abnormalities and Premature Death in Medicated Patients
Loren H. Crabbtree, Jr., M.D., Project Transition, 200 High Point Drive, Suite 213, Chalfont, PA 18914

Educational Objectives:
At the conclusion of this session, the participant should be able to: (1) define the Metabolic Syndrome & its frequency in patients with mental illness; (2) describe causal factors of the Metabolic Syndrome that account for its high frequency in these patients; (3) identify three or more intervention strategies and describe their associated outcomes.

Summary:
Introduction: the average lifespan of adults with serious and persistent mental illness (SPMI) is 20% less than that of American adults. The major causes are diabetes and arteriosclerosis-related illnesses. The presence of the Metabolic Syndrome is highly associated with their emergence.

Methods: in this 18-month self-funded study, 105 adults with SPMI were evaluated quarterly for the five component abnormalities of the Metabolic Syndrome. Findings were compared with those of a national sample (NHANES III). Patients self-selected among four intervention groups, two of which included lifestyle modification (one with and another without the use of pharmaceutical aids Orlistat and Metformin). Impact upon weight was assessed quarterly.

Results: the presence of the Metabolic Syndrome in the sample was 46%, over twice the national prevalence that has been declared epidemic for persons 20–59 years of age (p<0.0001). Abdominal obesity, triglyceride, and HDL levels were significantly higher (p<0.0001), FBS and BP were not. 68% of patients in the lifestyle-change group lost weight quarterly—an average of 5 lbs./quarter; 74% of those in the group that additionally used pharmaceutical aids lost weight quarterly—an average of 8 lbs./quarter; and 59% of individuals who were in neither group gained weight quarterly—an average of 4 lbs./quarter (59%).

Conclusions/Discussion: the sample’s over-representation of the Metabolic Syndrome has multiple causal factors. It is vital for
patients and professionals to become aware of health vulnerabilities associated with SPMI and its treatments, as well as the strategies that offset illness progression and premature death.

References:

NR546  Tuesday, May 4, 3:00 p.m.-5:00 p.m.
Impact of Open Access to Atypical Antipsychotics in California Medicaid
Supported by Eli Lilly and Company
Jeong Hoon Ahn, Ph.D., University of Southern California, Pharm Economics Department, 1540 E. Alcazar, Room CHP#140, Los Angeles, CA 90089-9004; Jeffery S. McCombs, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize how open access to atypical antipsychotics has impacted the cost of treating medical patients with severe mental disorders.

Summary:
Objective: Investigate the impact of open access to atypical antipsychotics on the cost of treating patients with severe mental disorders.

Methods: Monthly cost data were derived for two cohorts of California Medicaid patients with severe mental illness. The intervention cohort (N=92,089) utilized services over the 24-months spanning the repeal of prior authorization in October 1997. The control cohort (N=75,551) used services spanning October 1995. Multivariate time trend models for each service category were estimated to test whether utilization patterns were altered after open access.

Results: The unadjusted rate of growth for each type of service in the control cohort was (-0.8% + 1.8%) compared with (0.0 + 3.5%) for the intervention cohort. The multivariate time trend models for all services found that total cost and long term care use increased in the first 2 months after open access by 4% and 3%, respectively, but consistently decreased in the next 10 months and 8 months, respectively. The estimated total cost savings from these changes in utilization patterns was $145.50 per patient per month over the 12-month period following open access.

Conclusion: These results suggest that policy analysts must be careful when evaluating open access to atypical antipsychotics since short-term and long-term impacts on cost may differ.

References:

NR548  Tuesday, May 4, 3:00 p.m.-5:00 p.m.
Unmet Need for Mental Health Services in Europe: Results From the ESEMED Project
Jordi Alonso, M.D., Health Services, IMIM Institute Municipal, Drive Aiguader 80, Barcelona E-08003, Spain; Miguel Codony, Tery Brugha, Viviene Kouess, Mathias C. Angermeyer, Gabriella Polidori, M.D., Steven Katz

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the frequency of use of formal health services and recognize the frequency of unmet need for psychiatric disorders.

Summary:
Objective: High prevalences of mental disorders in epidemiological studies have fueled controversy about the assessment of need for care. We estimated unmet need for care in Europe based on the ESEMeD project.

Method: Conducted in Belgium, France, Germany, Italy, the Netherlands, and Spain. 21,425 individuals aged 18+ years not institutionalized participated (61% response) in a home computer-assisted interview. Unmet need was estimated as the proportion with no formal services visits, no contact with a mental specialist,
and not appropriate treatment, among those with any and those with a significantly disabling DSM-IV 12-month disorder.

Results: 6.4% of the total sample reported using mental health services in previous year. Among those with any 12-month disorder (10%), 74% did not use the formal services, 84% did not visit a mental specialist, and 87% did not receive appropriate treatment. For those with any significantly disabling disorder (6%), figures were 70%, 81%, and 70%, respectively. Unmet need for those with significantly disabling 12-month major depression episode (2%) was: 56%, 72%, and 76%, respectively.

Conclusion: Although the level of need varies substantially according to the criterion used, unmet need for care is high in Europe.

Funding: EU Commission (QLG5-1999-0142), GSK.

References:

NR549 Tuesday, May 4, 3:00 p.m.-5:00 p.m.
Can Pharmacy Data Identify Patients With Serious Mentally Illness Needing Help With Adherence?

Emily M. Wollmann, M.S.W., Smitrec, VA Ann Arbor Health and Care System, PO Box 130170, Ann Arbor, MI 48113-0170; Patricia Schraner, M.S.W., John E. Zeber, M.H.A., Janet Kavanagh, M.S., Marcia T. Valenstein, M.D.

Educational Objectives: At the conclusion of this session, the participant should be able to recognize ways in which administrative data might be used in organized systems of care to identify patients with serious mental illness that may require additional outreach and intervention for medication adherence.

Summary: Objective: Patients with serious mental illness and poor adherence are at increased risk for relapse. Health care systems could potentially use administrative data to identify at-risk patients. We examine the usefulness of administrative data for this purpose. Methods: We used administrative data from two VAs to identify patients with schizophrenia/schizoaffective disorder who filled <80% of the oral antipsychotics needed for 12-month coverage (N=537). We reviewed medical charts to determine the current diagnoses recorded in physician notes and potential explanations for patients' failure to fill antipsychotics, such as transferring care or starting long-term deports. We also determined whether patients were already receiving of common interventions to improve adherence.

Results: 87% (n=487) of flagged patients had a chart diagnosis of schizophrenia/schizoaffective disorder, and 75% of these patients had no explanations for irregular antipsychotic fills. Thus 65% (n=350) of flagged patients could be considered "true positives" for a schizophrenia/schizoaffective diagnosis and poor adherence. Only 19% of these at-risk patients were receiving strong interventions to improve adherence.

Conclusions: Few "true positive" patients in the sample are receiving strong interventions to improve adherence. Administrative data is a useful first screen to identify poor antipsychotic adherence among patients with schizophrenia but must be followed by further chart/case management screens before patient intervention.

Funding Source(s): Department of Veterans Affairs Health Services Research and Development (HSR&D) Investigator-Initiated Research (IIR) #01-074-1

References:
NR551  Tuesday, May 4, 3:00 p.m.-5:00 p.m.  
Comparison of First Refill Rates Among Branded SSRI Users  
Supported by Pfizer Inc.  
C. Daniels Mullins, Ph.D., PHSR, University of Maryland, 515 West Lombard Street-2nd Floor, Baltimore, MD 21201; Fadia T. Shaya, Ph.D., Fanlun Meng, M.S., Junling Wang, M.S., Morgan S. Bron, Pharm.D.  

Educational Objectives:  At the conclusion of this session, the participant should be able to: (1) examine differences in patterns for first refill prescriptions across branded SSRI therapies; (2) explore factors that impact the likelihood of first refill; (3) discover how logistic regression can distinguish the simultaneous impact of choice of SSRI and covariates on first refill patterns.  

Summary:  
Objective: Prior research documents that discontinuation rates among serotonin reuptake inhibitor (SSRI) users are high, but little is known about the likelihood of refilling at least one prescription. This study compares rates of first refills across SSRIs that remain on patent.  
Method: This retrospective cohort study used an administrative database from January 1, 1999 to June 30, 2002. Patients were followed up to six months after the first branded SSRIs. Refill was defined as refilling the first prescription for SSRIs of interest within 15 days or 1.5 times days supply. Logistic regression and sensitivity analyses examined the impact of age, gender, and copayment as covariates.  
Results: Based on descriptive analyses, sertraline patients (N=5,590; 54.70% refill; p=0.0001) and citalopram patients (N=4,124; 54.49% refill; p=0.0008) were more likely to have a refill than paroxetine patients (N=5,201; 50.99% refill). These results were consistent with the logistic regressions where covariates were significant at the p < 0.10 but not the p < 0.05 level.  
Conclusion: The likelihood of refilling an SSRI varies by the specific SSRI and may vary by age, gender, and copayment amount. Patients are more likely to refill the first prescriptions for sertraline or citalopram than for paroxetine.  
Funding Source(s): Pfizer Inc.  

References:  

NR552  Tuesday, May 4, 3:00 p.m.-5:00 p.m.  
Anxiolytics Impact Antidepressant Treatment Adequacy  
Jeffrey B. Weilburg, M.D., Department of Psychiatry, Massachusetts General Hospital, 815 ACC, 55 Fruit Street, Boston, MA 02114; Kathleen M. O’Leary, B.A., Randall S. Stafford, M.D., Stan F. Finkelstein, M.D., Maurizio Fava, M.D.  

Educational Objectives:  At the conclusion of this session, the participant should be able to understand the impact of the use of anxiolytic medications on patterns of use of antidepressants.  

Summary:  
Background: Individuals experiencing major depressive disorder (MDD) with high levels of anxiety symptoms were found to be less likely to respond to antidepressant treatment. Little is known about the impact, if any, of the use of anxiolytic medications (AMs) on the treatment of depression.  
Methods: Using medical and pharmacy claims from a commercial HMO, we selected patients who were prescribed ADs, (n=169,277, June 1999–December 2002), sorted them by claims diagnosis (depression alone, anxiety alone, and depression plus anxiety), and then by medication use (AD alone or AD + AM (selected benzodiazepines and Buspirone). We determined the rate of minimally adequate AD treatment for patients in each subgroup.  
Results: Patients with a diagnosis of depression only: ADs alone: adequacy = 57.6% (2207/3830); ADs plus AMs: adequacy = 67.1% (1422/2120).  
Patients with a diagnosis of depression plus anxiety: ADs alone: adequacy = 55.2% (647/1172); ADs plus AMs: adequacy = 66.1% (1123/1700).  
Patients with a diagnosis of anxiety alone: AD alone adequacy = 45.3% (742/1636); ADs plus AMs adequacy = 52.2% (928/1778).  
Conclusions: Patients prescribed AMs had higher rates of AD treatment adequacy than patients prescribed ADs alone, independent of diagnosis of depression or anxiety. This raises the interesting suggestion that AM use may positively impact AD use patterns perhaps by addressing both symptoms of depression and side-effects of antidepressants.  

References:  

NR553  Tuesday, May 4, 3:00 p.m.-5:00 p.m.  
Diagnosis and Treatment Adequacy for Patients Receiving Antidepressants  
Jeffrey B. Weilburg, M.D., Department of Psychiatry, Massachusetts General Hospital, 815 ACC, 55 Fruit Street, Boston, MA 02114; Kathleen M. O’Leary, B.A., Randall S. Stafford, M.D., Stan F. Finkelstein, M.D.  

Educational Objectives:  At the conclusion of this session, the participant should be able to recognize that only a small portion of patients treated with antidepressants receive a claims diagnosis of depression.  

Summary:  
Background: Patients without a claims diagnosis of depression are typically overlooked when the quality of depression care and/or antidepressant (AD) use in general medical settings is evaluated.  
Methods: Medical and pharmacy claims from patients (n=169,277) in a commercial HMO were used to determine the rate at which patients treated with ADs received a claims diagnosis of depression, the correlation between diagnosis of depression and minimally adequate AD treatment, and the correlation between a depression diagnosis and seeing a psychiatrist.  
Results: The rate of depression diagnosis in patients: a) who received an AD: 37.8% (8822/23,390), b) who saw a psychiatrist: 74% (6291/8511), and c) who never saw a psychiatrist: 17% (2531/14,879). The rate of AD adequacy in all patients using ADs: 49.0% (11,452/23,390), patients with diagnosis of depression: 61.2%
when the adequacy of AD treatment is evaluated, a large portion
of patients treated with ADs not seen by a psychiatrist (e.g. cared for solely in a general
medical setting) tended not to get a diagnosis of depression. If a
claims diagnosis of depression is required for patient inclusion
when the adequacy of AD treatment is evaluated, a large portion
of patients treated with ADs, especially those seen only in non-
psychiatric settings may be excluded from consideration.

References:
1. Spettell CM, Wall TC, Allison J, et. al: Identifying physician-
recognized depression from administrative data: conse-
quences for quality measurement. Health Serv Res. 2003;
2. Weilburg JB, O’Leary KM, Meigs JB, Hennen J, Stafford RS:
Evaluation of the adequacy of outpatient antidepressant treat-

NR554 Tuesday, May 4, 3:00 p.m.-5:00 p.m.
Feasibility of Pragmatic Trials in Psychiatry: A Case From the Netherlands
Bea Tiemens, Ph.D., GRIP, Gelderste Roos, PO Box 27, Renkum 6870 AA, Netherlands; Marianne C. Donker, Ph.D., Annemiek Van Straten, Ph.D., Leona Hakkaart, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be
able to consider the external and internal validity of pragmatic
randomized clinical trials.

Summary:
Objective: To contribute to the debate on the external validity
of traditional randomized clinical trials (RCT’s), the focus of this
presentation is the feasibility and scientific consequences of prag-
matic trials in psychiatry.
Method: We present an example of a large scale, multi center
pragmatic trial on the cost-effectiveness of three therapeutic ap-
proaches for patients with an anxiety or depressive disorder. The trial was carried out in non-academic mental health care settings in the Netherlands.
Results: We met considerable problems while encountering the study: much slower intake than estimated by the mental health institutes led to recruitment of new institutes, adaptations to the randomization scheme and shortening of the follow-up period; different waiting lists for patients led to setting restrictions in waiting time for the conditions; and overlap in treatment conditions and poor adherence to the randomized conditions. Finally, we suc-
cceeded in successful randomization, sufficient power, limited drop out from the study, and compared to clinical practice, normal drop out from therapy.
Conclusion: In this pragmatic trial we reached high external
validity with a trade-off to internal validity. The optimal balance
between external and internal validity was yet not found.

References:
1. Spettell CM, Wall TC, Allison J, et. al: Identifying Physician-
recognized depression from administrative data: conse-
quences for quality measurement. Health Serv Res. 2003;
38(4):1081-1102.
2. Weilburg JB, O’Leary KM, Meigs JB, Hennen J, Stafford RS:
Evaluation of the adequacy of outpatient antidepressant treat-

NR555 Tuesday, May 4, 3:00 p.m.-5:00 p.m.
Comorbid PTSD and Alcohol Abuse in Veterans With Elevated Depression Scores
Steven K. Dobscha, M.D., Portland VA Medical Center, PO Box 1034 (P3MHDC), Portland, OR 97207; Kathryn Corson, Ph.D., Martha Gerrity, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be
able to demonstrate improved knowledge of the prevalence and
importance of active PTSD and alcohol abuse in patients with
elevated depression measure scores in VA primary care settings.

Summary:
Objective: To examine the prevalence of posttraumatic stress
disorder (PTSD) and alcohol abuse in veterans treated in a primary
care setting who have elevated depression measure scores.
Methods: 400 patients with Patient Health Questionnaire (PHQ)
depression scores ≥10 (indicating moderate or greater depression
severity) were recruited for a randomized trial of a collaborative
intervention for depression in primary care. Exclusion criteria were
treatment from a mental health specialist within the prior six
months, or documented cognitive disorders, psychotic symptoms,
or terminal illness. 380 participants completed both the Alcohol
Use Disorders Identification Test (AUDIT/AUDIT-C) and Post-
traumatic Stress Disorder Checklist (PCL).
Results: 37% of participants had PCL scores ≥ 50 indicating
probable and active PTSD. Forty-two percent reported no current
alcohol consumption. However, among participants who did drink,
411 had AUDIT-C scores ≥4, indicating a high likelihood of active
alcohol abuse. Overall, 10% of participants had scores suggesting
both active PTSD and alcohol abuse.
Conclusion: Active PTSD and alcohol abuse are very common
in veterans presenting with depression symptoms in primary care
settings. Veterans with elevated depression measure scores
should be routinely assessed for these comorbid conditions to
ensure appropriate care.

Funding Source(s): Department of Veterans Affairs, HSRD
(Project MHI 20-020-1)

References:
1. Hankin CS, Spiro A, 3rd, Miller DR, Kazis L: Mental disorders
and mental health treatment among U.S. Department of Veter-
ans Affairs outpatients: the Veterans Health Study. Am J Psy-
2. Bush K, Kivlahan DR, McDonell MB, Fihn SD, Bradley KA: The
AUDIT alcohol consumption questions (AUDIT-C): an effective
158:1789–95.

NR556 Tuesday, May 4, 3:00 p.m.-5:00 p.m.
The Burden of Depression in Patients With Bipolar Disorder
Supported by GlaxoSmithKline
Alex Z. Fu, Pharmacy Department, University of North Carolina,
Chapel Hill, 205 B. Beard Hall, CB#7360, Chapel Hill, NC
27599–7360; Anupama A. Krishnan, M.S., Sonya D. Harris,
M.P.H.

Educational Objectives:
At the conclusion of this session, the participant should be
able to recognize the economic burden of bipolar depression and
mania.
Objective: To characterize depressive and manic episodes in a bipolar population in terms of frequency and economic burden to a managed care organization.

Methods: Using claims data (1998–2002) for a bipolar patient sample (ICD-9:296.4-296.8), we characterized episodes of care as depressive or manic based on ICD-9 codes and compared outpatient, pharmacy, and inpatient costs using t-tests and multivariate linear regression.

Results: During the study period, 13,118 subjects experienced 14,069 bipolar episodes. Annual outpatient bipolar depression costs were four times as high and inpatient bipolar depression costs were twice as high as those for bipolar mania. Depressive episodes occurred three times more frequently (N=3083) as compared to manic episodes (N=1236). The average outpatient, pharmacy and inpatient costs for a depressive episode were $1426, $1721, $1646 compared with $863 (p<0.0001), $1248 (p<0.0001), $1736 (p=0.54) for a manic episode. Controlling for age, gender, length of episode, site of index visit, and pre-episode costs, the cost of a bipolar depressive episode ($5503) was approximately twice as high as that of mania ($2842).

Conclusion: The economic burden of bipolar depression appears to be greater than that of mania. Preventing or delaying bipolar depression could result in potential cost savings to a managed care organization.

References:

NR558 Tuesday May 4, 3:00 p.m.-5:00 p.m.
What Is the Profile of the Noncompliant Patient? A Study in Outpatient Services
E. Munoz Marron, Ph.D., Psychiatry Department, San Carlos University Hospital, Martin Lagos S/n, Madrid 28040, Spain; Blanca Reneses, L.C.P., Juan J. Lopez-Ibor, Jr., M.D.

Educational Objectives:
At the conclusion of this session, the participant should know what the factors are that influence dropout of psychiatric patients. These factors can be related to the patients (sociodemographic, psychopathological conditions), to the treatment (type, frequency) or to the therapist (number of therapists and professional characteristics).

Summary:
Objective: Several studies have shown that treatment dropout in the outpatient psychiatric setting occurs in about 25% to 55% of cases. Given the importance of continuity of care, the identification of factors that can influence treatment dropout is also of major importance.

Methods: The total one-year incidence of patients in a catchment area in Madrid (Spain) was studied. The total sample of all patients that abandoned treatment during the following two years (n=789) was compared with a control group of the same size randomly from the same catchment area and period. Variables studied included sociodemographic, clinical, treatment and therapist-related characteristics. Statistical analysis was done with bivariant and multiple regression tests.

Results and Conclusions: Dropout rate was 33%. The higher dropout rates were found among the younger patients, with primary and secondary education, with diagnosis of drug dependences, personality or eating disorders. Patients without pharmacological treatment, without psychiatric antecedents, or many therapist implicated along the treatment had a high dropout. Multiple logistic regression analysis identified the following predictors of treatment dropout: age<35, female sex and living alone, presently working, no psychiatric history and having had more than one doctor or therapist in the same illness episode.

References:
NR559  Tuesday, May 4, 3:00 p.m.-5:00 p.m.
Geophysical Variables and Psychiatric Outpatient Attendance: Beyond Lunar Hypothesis
Parameshwaran Ramakrishnan, D.P.M., Dementia Society of GOA, 12-117 P&T Colony Dilsukhnagar, Hyderabad, AP 500060, India; Thennarasu Kandavel, Ph.D., Chittaranjan Andrade, M.D., John Fernandes, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize that the moon may be a confounding factor in the behavioral effects of geophysical variables. Disregarding this field of inquiry because it is replete with myths is an understandable but inappropriate scientific response.

Summary:
Objective: We examined whether lunar and other geophysical variables influence outpatient (OP) attendance, a proxy variable for onset or worsening of mental illness.
Method: Daily numbers of first OP attendance was examined between Jan 1, 1990 to Jan 31, 2001, to assess whether this variable was related to 15 parameters of lunar, solar, climatic, and other geophysical activity. Diagnoses of interest were non-affective psychoses, mania, depression, and minor mental disorders (MMD).
Results: Study selection criteria were met by 30,195 patients. Variables most significantly associated were solar radio flux (RF) below 800 MHz and geomagnetic activity (GMA). While RF affected all the diagnostic groups, GMA was significantly associated with MMD and total cases only. Sine wave curve of admissions upon time filled on the lunar cycle starting with new moon showed a significantly higher number of psychosis and total cases around 21st day. Lunar cycle was associated only with GMA among geophysical variables. Significant relationships notwithstanding, the percentages of variance were very small. Various other solar, lunar, and climatic variables significantly related to the diagnostic groups are discussed.
Conclusions: RF and GMA were found to influence first-time psychiatric OP attendance. These findings need replication and further study. Where as RF, GMA and other variables may exert physiological effects they may be acting as confounding factors in the lunar causation myth of mental illness.
Funding Source(s): NIL

References:

NR560  Tuesday May 4, 3:00 p.m.-5:00 p.m.
Health Care Utilization in Bipolar Depression and Mania
Supported by GlaxoSmithKline
Paul Stang, Ph.D., Galt Associates Incorporated, 640 Sentry Parkway, Suite 305, Blue Bell, PA 19422; Anupama A. Krishnan, M.S., Marianne Ulickcas-Yood, D.Sc., Gena Kucera, M.P.H., Karen Wells, B.S., Cathrine Frank, M.D.

Educational Objectives:
At the conclusion of this session, the participant should understand patterns of healthcare use in bipolar depression and mania.

Summary:
Objective: To compare health care resource utilization in the three years prior to and one year following initial diagnosis of bipolar depression vs. bipolar mania.
Methods: We identified a cohort of 1,645 patients newly diagnosed with bipolar disorder in a large Midwestern health system from January 1,2000, through August 30, 2002. Patients were classified as depressed (ICD 296.50–56), manic (296.40–46), or unspecified (296.80–89) bipolar based on the ICD-9 code at their initial bipolar visit.
Results: The mean number of patient encounters following a diagnosis of bipolar disorder was 12.5 outpatient 0.8 emergency room, and 0.4 inpatient per patient per year. The mean number of patient encounters for outpatient, emergency room, and inpatient services was higher for bipolar depression compared with mania, with greatest differences occurring in emergency room encounters. More bipolar depressed subjects accessed emergency department (40.9% vs 34.0%), inpatient mental health (12.5% vs 10.3%) and any mental health service (74.7% vs 69.2) compared with manic subjects. The utilization pattern for bipolar unspecified subjects was similar to manic subjects.
Conclusion: Bipolar depressed patients appear to have higher rates of health care utilization compared with those with bipolar mania.
Funding Source(s): Research funded by GlaxoSmithKline

References:

NR561  Tuesday, May 4, 3:00 p.m.-5:00 p.m.
The Economic Impact of Mood Stabilizers in Bipolar Disorder
Supported by GlaxoSmithKline
W. Robert Simons, Ph.D., Global Health Incorporated, 41 River Road, Summit, NJ 07901; Anupama A. Krishnan, M.S.

Educational Objectives:
At the conclusion of this session, the participant should be able to demonstrate the pharmaeconomics of the management of bipolar disorder in managed care.

Summary:
Objective: To provide real-world evidence of the economic value of lamotrigine as a mood stabilizer for bipolar disorder.
Methods: Using managed care claims data (1997–2001) for a bipolar patient sample, we compared hospitalization rates, medical and pharmacy costs 12 months pre and post initiation of lamotrigine in patients previously treated with lithium, valproate/carbamazepine, other anticonvulsants, selective serotonin reuptake inhibitors (SSRIs), or other antidepressants.
Results: 406 bipolar patients who received at least one prescription for lamotrigine formed the study sample. Following the initiation of lamotrigine a statistically significant reduction in the number of hospitalized days due to acute depression in the lithium (17.41 days) and valproate/carbamazepine (9.41) cohort was observed alongside a non-significant reduction in other cohorts. Hospitalizations due to mania were too few for any meaningful analysis. The initiation of lamotrigine resulted in lower medical costs in patients previously treated with lithium ($19,230), carbamazepine valproate ($867), SSRIs ($4,453) and other antidepressants ($2,450). The net change in medical costs across the population...
was ($-1,275) while the net change in medication costs was $834 for a total new savings of $421 per patient per year.

Conclusions: The initiation of lamotrigine appears to be associated with reduction in hospitalization days and costs to managed care organizations.

Funding Source(s): GlaxoSmithKline

References:

NR562 Tuesday, May 4, 3:00 p.m.–5:00 p.m.
Persistence With Initially Prescribed Antipsychotics Supported by AstraZeneca Pharmaceuticals

W. Robert Simons, Ph.D., Global Health Incorporated, 41 River Road, Summit, NJ 07901

Educational Objectives:

At the conclusion of this presentation, the participant should be able to summarize and compare the rates of persistence over the first year of monotherapy with quetiapine versus olanzapine, risperidone, and haloperidol in patients receiving initial therapy for bipolar or psychotic disorders.

Summary:

Objective: To compare persistence (duration of initially prescribed monotherapy without addition, switching, or discontinuation) with quetiapine versus other antipsychotics.

Methods: From managed care claims data, 1294 patients with bipolar or psychotic disorders treated with quetiapine were matched with comparator groups treated with haloperidol, risperidone, or olanzapine. Persistence was assessed at 6, 9, and 12 months.

Results: At 6 months, persistence was greater with quetiapine (55%) than with haloperidol (33%, P<0.01), risperidone (51%, P=0.03), and olanzapine (51%, P=0.03). Persistence remained significantly greater with quetiapine than with haloperidol and risperidone at 9 months and with haloperidol at 12 months. There were significantly fewer discontinuations with quetiapine than with all comparators at all assessments. In the bipolar subset (n=775), 6-month persistence was greater with quetiapine (57%) than with haloperidol (42%, P<0.01) and risperidone (52%, P=0.04), and there were significantly fewer discontinuations with quetiapine than with all comparators at 12 months. Average quetiapine dosage was 342.8 mg/d; higher dosage was associated with improved persistence (P<0.01).

Conclusions: During the first year of treatment, persistence was greater with quetiapine than with other antipsychotics, and higher dosage contributed to improved persistence.

Funding Source(s): AstraZeneca Pharma.

References:

NR563 Tuesday, May 4, 3:00 p.m.–5:00 p.m.
Measurement of Psychiatrists’ Coordination in Split Treatment

Charles J. LoPiccolo, M.D., Psychiatry Department, University of Miami, 251 Hibiscus Avenue, Lauderdale-by-Sea, FL 33308-5453; C. Eldon Taylor, M.S., Carl Eisdofer, M.D., Cheryl L. Clemence, M.P.H.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the variability of compliance by psychologists to accepted standards for coordination of care and the issues related to non-compliance.

Summary:

Objective: Examine the adherence rates of psychiatrists with APA standards for coordination of care in split treatment.

Method: Coordination of care in split treatment is monitored from claims paid data in an academic MBO as an ongoing quality improvement activity. For an 18-month period 93 psychiatrists were identified with 559 patients in split treatment and were mailed a survey. Surveys were controlled for change of providers.

Results: Self report survey results were obtained from 69 psychiatrists for 295 patients in split treatment. The average rate of coordination was 66%; however, the distribution was bimodal with 36% of psychiatrists always coordinating and 26% never coordinating. Not obtaining a release accounted for 87% of non-coordination.

Conclusion: While coordination of care in split treatment is an APA standard of practice only one-third of psychiatrists fully complied. That one-third of patients in split treatment did not receive coordinated care suggests a need for improvement to meet the APA standards of practice and avoid legal exposure.

References:

NR564 Tuesday, May 4, 3:00 p.m.–5:00 p.m.
Health Care Utilization for Bipolar Disorder in a Managed Care Organization
Supported by Bristol-Meyers-Squibb

Russell L. Knoth, Ph.D., PE Outcomes, RX Solutions, 3515 Harbor Boulevard, LC07-264, Costa Mesa, CA 92626; Kristina Chen, M.S., Eskinder Tafesse, Ph.D.

Educational Objectives:

At the conclusion of this session, participants will know the extent of annual healthcare resources, both pharmacy and medical, incurred by patients diagnosed with bipolar disorder, compared to an average health plan member, in a managed care organization.

Summary:

Introduction: The purpose of this study was to determine the direct health care expenditures incurred by patients in a managed care organization diagnosed with bipolar disorder.

Method: Continuously enrolled adult patients with a medical claim with a diagnosis of bipolar disease between 7/1/00 and 6/30/01 were identified. All pharmacy and medical claims for these
patients were then examined in the one-year period following the index diagnosis. Results: A total of 4,397 patients met the inclusion criteria. The average age of the identified cohort was 53 years old, and 66.1% were female. Among these patients, a total of 91.3% were prescribed a psychotropic medication and average annual pharmacy costs, based on ingredient costs, totaled $1,940 per person. In addition, 29.7% of the patients had at least one hospital admission, 39.1% had at least one emergency department visit, and each patient averaged 10.6 outpatient visits. Average annual medical costs, based on submitted charges, totaled $30,811 per patient and direct healthcare expenditures for this cohort totaled more than $144 million. Conclusion: These results demonstrate that patients diagnosed with bipolar disorder are high utilizers of medical services compared to the average health plan member, which speaks to the need for creative and innovative programs to manage this population. Funding Source(s): This research was funded in part by Bristol-Myers Squibb.

**References:**


**NR565 Tuesday, May 4, 3:00 p.m.-5:00 p.m.**

**Reducing Recidivism: Telephonic Targeted Care Management in Academic MBHO**

C. Eldon Taylor, M.S. Psychiatry Department, University of Miami, 1150 NW 14th Street, Suite 501, Miami, FL 33136; Charles J. LoPiccolo, M.D.; Carl Eisdorfer, M.D., Cheryl L. Clemence, M.P.H.

**Educational Objectives:**

At the conclusion of this session, the participant should be able to objectively evaluate the clinical and economic impact of the telephonic targeted care management program and implement aspects of the program or replicate.

**Summary:**

**Objective:** The study evaluated the impact of a telephonic targeted care management program developed by an academic MBHO to reduce recidivism and cost of care of high-risk members with a history of multiple psychiatric hospitalizations with a cost-effective program. **Methods:** 60 high-risk members with two or more psychiatric hospitalizations in the 12 months prior to the program continuously enrolled for 24 months were selected. Measures were total admissions, bed days average lengths of stay, and cost of care pre and post intervention. Program blended elements of psychiatric case management with diseases management and telehealth care to improve adherence to post discharge treatment plans. Program interventions included appointment reminder calls and verification calls for each outpatient visit with all non-adherent members referred to telephonic care manager. **Results:** Program produced statistically significant reductions (p<.001) in admissions (171 pre, 42 post), bed days (771 pre, 168 post), and average length of stay (4.51 pre, 4.00 post). Cost of care savings averaged $3301 per person per year after subtracting program expenses. **Conclusions:** A telephonic targeted care management program was effective and cost effective. **Funding Source(s):** University of Miami

**References:**


**NR566 Tuesday, May 4, 3:00 p.m.-5:00 p.m.**

**Bipolar and/or Psychotic Comorbidity in ADHD and Autism Spectrum Disorders**

Christopher Gillberg, M.D., Goteborg University, Kungsportsan 12, Gothenburg 41119, Sweden; Maria Rastam, M.D., Henrik Soderstrom, M.D., Ola Stahlberg

**Educational Objectives:**

At the conclusion of this session, the participant should be able to discuss the comorbidity of bipolar disorder, schizophrenia, and other psychotic disorders in adults with childhood onset AD/HD and/or autism spectrum disorders.

**Summary:** **Background:** Individuals with attention-deficit/hyperactivity disorder (AD/HD) and autism spectrum disorders (ASD) often display symptoms from other diagnostic categories. Exclusion criteria in the DSM-IV and ICD-10 impede the use of categorical diagnoses to describe the particular problem constellation in a patient. **Method:** In this study, we describe the prevalence and patterns of comorbid bipolar and psychotic disorders in 241 consecutively referred adult patients with AD/HD and/or ASD. **Results:** Thirty percent of patients with AD/HD had comorbid ASD and 38% of patients with ASD had comorbid AD/HD. Of the subjects with ASD, 7.0% had bipolar disorder with psychotic features, and 8.5% had schizophrenia or another psychotic disorder. The corresponding figures for the patients with AD/HD were 5.0% and 4.3% respectively. **Conclusion:** Current criteria have to be revised to acknowledge the comorbidity of bipolar and/or psychotic disorders in AD/HD and ASD.

**References:**


**NR567 Tuesday, May 4, 3:00 p.m.-5:00 p.m.**

**Asperger's Disorder as a Negative Symptom Disorder: An Open Trial of Risperdal**

Elizabeth Sirota, M.D., Department of Psychiatry, Medical College of Georgia, 1515 Pope Avenue, Augusta, GA 30912; Donna L. Londino, M.D.; Jeffrey L. Rausch, M.D.

**Educational Objectives:**

At the conclusion of this session, the participant should be able to understand the potential role of the newer atypical antipsychotics in treating the social deficits seen in Asperger's disorder. **Objective:** To assess the efficacy of risperdone on negative symptoms and social interaction in patient's with Asperger disorder using standardized rating scales. **Method:** 12-week, open-trial pilot study of risperdone in 13 patients, ages six to 18, diagnosed with Asperger's disorder ac-
ing to DSM-IV criteria. Patients were screened using the structured clinical interview for diagnosis and the DSM-IV to exclude individuals with psychotic disorders, cluster A personality disorders, and other autistic disorders. Study design progressed from a fixed dose to a titrated dose paradigm. Outcome measures were determined at baseline, week 3, 6, 9, and 12 utilizing the Scale for Assessment of Negative Symptoms and several secondary outcome measures. Patients were monitored for safety and adverse events throughout the study.

Results: Open results of the primary efficacy measure, the Scale for Assessment of Negative Symptoms (SANS), indicated a significant reduction (50%) in negative symptoms at week six. The modified Asperger Syndrome Diagnostic Scale (ASDS) was examined as a secondary measure. Improvement was noted in all dimensions with significant improvements noted in social functioning at six to nine weeks of treatment. An initial increase in the Abnormal Involuntary Movement Scale (AIMS) during the first 3 weeks of the trial abated by week 9.

Conclusions: This prospective study suggests that the social impairments seen in Asperger’s disorder may respond to risperidone treatment. This is especially enlightening given prior suggestions that pharmacotherapy was unable to target the core deficits of the disorder. Clearly, additional open trial studies, as well as double-blind, placebo controlled studies are indicated to confirm these preliminary findings.

References:

NR568 Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Efficacy and Tolerability of Indiplon Modified Release in Elderly Patients With Chronic Sleep-Maintenance Insomnia
Supported by Neurocine Biosciences, Inc.
James K. Walsh, Ph.D., St. Luke’s Hospital, Unity Sleep Medicine, 232 South Woods Mill Road, Chesterfield, MO 63017; Alan Lankford, Ph.D., Andrew D. Krystal, M.D., Thomas Roth, Ph.D., Melinda Garber, B.A.

Educational Objectives:
The research presented will contribute to the participant’s understanding of the management of chronic insomnia in patients who may require treatment for four weeks or longer and the efficacy and safety of indiplon-IR, a new investigational therapy for insomnia.

Summary:
Objective: The efficacy and safety of immediate-release indiplon, a GABA potentiator, was evaluated in chronic insomnia patients in a five-week study.

Methods: Adults (N=194; 66% female; mean age, 40 years) who met DSM-IV criteria for primary insomnia for ≥ 3 months, confirmed by polysomnography (PSG), were randomized to five weeks of double-blind, parallel-group treatment with indiplon-IR-10mg, 20mg, or placebo. The primary endpoint was latency to persistent sleep (LPS) on PSG from the first two nights of therapy. Outcomes included latency to sleep onset (LSO), Digit Symbol Substitution Test (DSST), Symbol Copying Test (SCT), a Visual Analog Scale of sleepiness (VAS), sleep quality, and the Benzodiazepine Withdrawal Questionnaire (BWSQ).

Results: Indiplon-IR significantly reduced LPS on the 10mg dose (28 mins; p<0.002) and 20mg dose (27 mins; p<0.05) compared to placebo (37 mins), and improvement was sustained over the course of the study. LSO and sleep quality were significantly improved for both doses. There were no differences between indiplon-IR and placebo in next-day DSST, SCT or VAS effects; no evidence of withdrawal on the BWSQ; and no evidence of rebound insomnia.

Conclusions: Indiplon-IR was effective in chronic insomnia, improving sleep quality and showing no tolerance, and no evidence of discontinuation withdrawal or rebound.

Funding Source(s): Neurocine Biosciences

References:
NR570  Wednesday, May 5, 12:00 p.m.-2:00 p.m.
AIMS and ESRS: Cross-Scale Comparison to Define Simplified Criteria for Tardive Dyskinesia
Supported by Janssen Pharmaceutica and Research Foundation

Georges Gharabawi, M.D., CNS Medical Affairs, Janssen Pharmaceutica Products, L.P., 1125 Trenton-Harbourton Road, Titusville, NJ 08560; Cynthia Bossie, Ph.D., Ibrahim Turkoz, M.S., Stephen Rodriguez, M.S., Courtney Lonlyna, Robert Lasser, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to describe the concordance between the AIMS and ESRS dyskinesia scores for identifying tardive dyskinesia.

Summary:
Introduction: Tardive dyskinesia (TD) is the focus of numerous research reports, with different criteria generally based on AIMS or ESRS. This analysis addressed cross-validation of these scales and the need for a simple TD criterion.

Methods: Baseline data were combined from two studies using the AIMS and ESRS at the same visits. Regression models explored the relationship between AIMS and ESRS dyskinesia scores, plus global dyskinesia ratings on each scale. Concordance between the scales for identifying TD (mild symptoms on ≥2 items or moderate symptoms on ≥1) was tested and simplified criterion for predicting AIMS-defined TD by ESRS scores was studied.

Results: Data were available for 230 patients. Regression analyses showed a strong association between AIMS total and the ESRS dyskinesia scores and among the corresponding items of each scale. Cross-tabulation between AIMS- and ESRS-defined TD showed agreement for 95.7% (220/230) of observations. The ESRS CGI-S of dyskinesia was the best single predictor of AIMS-defined TD. A score ≥4 was associated with a ≥95% probability of AIMS-defined TD.

Conclusions: Data suggest a significant relationship between AIMS and ESRS dyskinesia scores, with high agreement for identifying TD. Results suggest the ESRS CGI-S of dyskinesia is a useful predictor of AIMS-defined TD.

Funding Source(s): Supported by Janssen Pharmaceutica Products, L.P.

References:

NR571  Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Insight in Stable Patients With Schizophrenia Receiving Long-Acting Risperidone
Supported by Janssen Pharmaceutica and Research Foundation

Georges Gharabawi, M.D., CNS Medical Affairs, Janssen Pharmaceutica Products, L.P., 1125 Trenton-Harbourton Road, Titusville, NJ 08560; Xavier Amador, Ph.D., Cynthia Bossie, Ph.D., Young Zhu, Ph.D., Robert Lasser, M.D.

Educational Objectives:
At the conclusion of this session, the participant should have a better understanding of the relationship between level of insight and measures of clinical and functional status in schizophrenic patients treated with long-acting injectable risperidone.

Summary:
Objective: To examine the relationship between level of insight and measures of clinical and functional status.

Methods: In an open-label study, patients with schizophrenia received long-acting injectable risperidone (25, 50, or 75 mg) every two weeks for up to 50 weeks. The Positive and Negative Syndrome Scale (PANSS) was used to assess level of insight and psychotic symptoms. Insight scores were correlated to PANSS total subscale scores, Clinical Global Impressions-Severity (CGI-S) ratings, and functional scores on the Short-Form 36 Health Survey (SF-36).

Results: Data were available for 614 patients. Mean insight scores significantly improved from 2.7 ± 1.5 at baseline to 2.5 ± 1.5 at endpoint (P=0.0002). Improvements in insight were positively and significantly correlated to improvements in both CGI-S ratings (r = 0.368; P<0.001) and PANSS subscale scores (positive symptoms, r = 0.397, P<0.001; negative symptoms, r = 0.369, P<0.001; anxiety and depressive symptoms, r = 0.238, P<0.001). SF-36 scores significantly improved (P<0.05) in patients with either improved or unchanged insight scores at endpoint.

Conclusion: The findings suggest a positive relationship between improvements in insight and improvements in clinical symptoms and functional status. Additional research is warranted.

Funding Source(s): Supported by Janssen Pharmaceutica Products, L.P.

References:

NR572  Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Direct Switch From Atypical Antipsychotics to Long-Acting Injectable Risperidone
Supported by Janssen-Cilag GMBH

Wim J. Arnoldussen, M.D., GGzE Case Management, Buitendijklaan 23, Eindhoven 5611 NG, Netherlands; Roland Vauth, M.D., Johan E. Kusters, M.D., Daniel Braendle, Ph.D., M.A. Lattf, M.D.

Educational Objectives:
This poster was written to share the knowledge gained from a clinical trial in stable patients suffering from schizophrenia and schizoaffective disorder treated with oral atypical antipsychotics who were switched directly to an injectable long-lasting antipsychotic formulation.

Summary:
Objective: To investigate the maintained efficacy and safety of risperidone long-acting injectable in previously stable patients with schizophrenia and other psychotic disorders switched directly from oral or depot antipsychotics. A subgroup analysis assessed patients switched from atypical antipsychotics.

Methods: Adult patients stable on their antipsychotic regimen for 150 days were switched to Risperidone long-acting (25 mg, increased to 37.5 mg or 50 mg, if necessary) injected at 14-day intervals for six months.

Results: 89 schizophrenic patients and 22 patients with schizoaffective disorder were analysed. Previous antipsychotic treatment included risperidone (78%), olanzapine (19%), and quetiapine (12%).
NR573  Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Evaluation of a Weight-Management Behavioral Program for Patients With Severe Mental Illness at 36 Months
Supported by Eli Lilly and Company

John Pendlebury, M.S.C., Department of Psychiatry, Cromwell House, Cromwell Road Eccles, Manchester M30 0Q7, England; Josepha Malone, R.G.N., Serdar Dursun, Ph.D., Som D. Soni, Ph.D., Peter M. Haddad, M.D.

Educational Objectives:
Attendees will gain enough knowledge to be able to set up a behavioral weight management clinic to improve the physical health of their patients. The poster would provide a networking opportunity for the author to share and exchange research on this important topic.

Summary:
Introduction: There have been growing physical health concerns about weight gain and psychotropic medication and its impact on compliance. This poster describes the setting up of a weight management clinic for patients with severe mental illness and evaluating its impact at 36 months.

Method: A behavioral intervention was developed which included educating the patient about weight loss, weight management, advising about healthy eating and exercise. Sessions were in groups, weekly, lasting one hour and comprised of an 8-week rotational cycle. Patients self referred.

Results: At 36 month, 70 patients were available for evaluation. The mean BMIs for patients attending the programme was 32.5 weight gain and reduced the need to change medication. The programme has reduced patients' and clinicians' concerns about weight loss, with a mean rate of -0.3 kg per session (SD 0.3). Subjectively, the patients achieved a mean weight loss of 5.0 kg (SD 5.5) at 36 months. Mean number of sessions attended was 33.7 (SD 34.9).

Conclusions: Directly switching to Risperidone long-acting was associated with further improvement in patients stable on oral atypical antipsychotic, offering a potential to enhance treatment quality.

Funding Source(s): Janssen-Cilag

References:

Funding Source(s):
Eli Lilly and Company.

NR574  Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Quetiapine: Greater Improvements in Tardive Dyskinesia Versus Haloperidol
Robin A. Emsley, M.D., Department of Psychiatry, University Stellenbosch, PO Box 19063, Tygerberg Cape Town 7505, South Africa; Jaori Turner, M.B., Juan Schronen, M.B., Karlien Botha, M.B., Retha Smit, R.N., Piet P. Oosthuizen, M.B.

Educational Objectives:
At the conclusion of this session, the participant should be able to: (1) compare the efficacy and tolerability of quetiapine and haloperidol in treating patients with schizophrenia or schizoaffective disorder and established tardive dyskinesia; (2) show that improvements in tardive dyskinesia are greater with the atypical antipsychotic quetiapine compared with the conventional antipsychotic haloperidol.

Summary:
Objective: Atypical antipsychotics have reduced propensities for producing acute extrapyramidal symptoms (EPS) and possibly tardive dyskinesia (TD), and may be effective in treating patients with established TD.

Methods: This 12-month, randomized, investigator-blinded study compared the efficacy of quetiapine (“Seroquel”) [n=22] with haloperidol (n=23) in treating patients with schizophrenia or schizoaffective disorder and established TD. Dyskinesia was assessed using the Extrapyramidal Symptoms Rating Scales (ESRS) dyskinesia subscale scores and the Clinical Global Impression (CGI) dyskinesia scores. Other EPS, weight, serum prolactin, and glycosylated hemoglobin were also assessed.

Results: Mean endpoint doses were 400 mg/day quetiapine and 8.5 mg/day haloperidol. Compared with haloperidol, the quetiapine group showed significantly greater improvements in ESRS dyskinesia (6 and 9 months [p<0.01]) and CGI dyskinesia (from 6 months onwards), and with repeated measures analysis (p=0.002). Response rate (≥50% symptom reduction) was greater with quetiapine than haloperidol (64% and 37% [8 months]: 55% and 28% [12 months]). Other EPS decreased significantly with quetiapine. Endpoint serum prolactin levels reduced with quetiapine but increased with haloperidol (p=0.005). No significant changes in weight or glucose metabolism were recorded in either group.

Conclusions: Quetiapine effectively reduces the severity of TD and is also well tolerated in patients with established TD.

References:
NR576  Wednesday, May 5, 12:00 p.m.-2:00 p.m.
A Controlled Trial of Extended-Release Bupropion in Adult ADHD
Supported by GlaxoSmithKline
Timothy E. Wilens, M.D., Department of Child Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC 725, Boston, MA 02114; James J. Hudziak, M.D., Daniel F. Connor, M.D., Barbara R. Haight, Pharm.D., Joseph P. Horrigan, M.D., Kenneth H. Hampton, B.S., Nathalie E. Richard, M.S., Jack G. Modell, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize that once-daily treatment with doses up to 450 mg/d of bupropion XL was efficacious and well-tolerated in this eight-week prospective clinical trial of adults with ADHD.

Summary:
Objective: To evaluate the efficacy and tolerability of a once-daily preparation of a nonstimulant, extended-release bupropion (bupropion XL), in adults with attention-deficit/hyperactivity disorder (ADHD).

Methods: A multi-site, placebo-controlled, parallel-group, 8-week prospective study of 162 subjects (ages 18–60 years) was undertaken in DSM-IV diagnosed adults with all subtypes of ADHD. Subjects were treated with up to 450 mg/d of bupropion XL and were rated on multiple outcomes weekly.

Results: Subjects receiving bupropion XL manifested significant improvement on the primary outcome measure, a reduction of ≥ 30% in the ADHD Rating Scale as assessed by investigators, over subjects receiving placebo as early as week 2 (p=0.01), which persisted through week 8 (p = .004). At endpoint, the self-reported Connors Rating Scale scores revealed that bupropion XL provided sustained benefit throughout the day compared to placebo (morning p=0.033, afternoon p=0.004, and evening p=0.024). Only 5% of subjects discontinued because of adverse effects related to the medication. There was no significant difference between bupropion XL and placebo in the incidence of adverse effects.

Conclusions: Once-daily bupropion XL is an effective and well-tolerated nonstimulant treatment for adults with ADHD.

References:

NR577  Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Substance Abuse in Juvenile Bipolar Disorder: Results From an Ongoing, Controlled Study National Institute on Drug Abuse
Timothy E. Wilens, M.D., Department of Child Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC 725, Boston, MA 02114

Educational Objectives:
At the conclusion of this session, the participant should be able to understand the risk juvenile BPD begets on SUD and to appreciate developmental variation in the presentation of BPD as it relates to SUD.

Summary:
Objective: Previous work in adults and youth has suggested that early onset bipolar disorder (BPD) is associated with an elevated risk for substance use disorders (SUD). No prospectively collected data have been available to evaluate this supposition. We now report on a mid-point analysis (103 of 230 cases to be recruited) of an ongoing, controlled, prospective, family based study of adolescents with and without BPD to evaluate the risk for SUD.

Methods: We systematically studied probands (aged 11–18 years) with BPD and compared them to a similarly ascertained group of youth without a mood disorder. Structured psychiatric interviews and multiple subjective and objective measures of SUD were collected. We evaluated specifically the relationship between SUD and the age at onset of BPD (prepubertal vs adolescent onset) and the presence of comorbid conduct disorder. We report on 103 cases.

Results: Youth were a mean age of 13.5 (±2.4) years and did not differ by group for any clinical characteristics or demographics. SUD was found in 32% of BPD youth compared to 7% of controls (Z=2.9, p=0.004). BPD youth ubiquitously had higher rates of additional comorbidities and poorer neuropsychological functioning than controls. Youth with the onset of their BPD in adolescence were at higher risk for SUD compared to those with the onset prepubertally (X2=9.3, p=0.002). Comorbidity with conduct disorder did not account for BPD as a risk factor for SUD (OR = 5.4 accounting for conduct).

Conclusions: The current mid-point findings from an ongoing study of BPD in youth replicate previous work indicating that juvenile BPD is a risk factor for SUD that was not accounted for by conduct disorder or other comorbid psychopathology. Youth with...
the onset of their BPD during adolescence were at particularly high risk for SUD.

Funding Source: NIDA.

References:

**NR578** Wednesday, May 5, 12:00 p.m.-2:00 p.m.
**Do Children and Adolescents With ADHD Respond Differently to Atomoxetine?**
Supported by Eli Lilly and Company

Timothy E. Wilens, M.D., Department of Child Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC 725, Boston, MA 02114; Jeffrey H. Newcorn, M.D., Christopher J. Kratochvil, M.D., Haitao Gao, Ph.D., Douglas L. Gelowitz, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize: (1) if there are similarities or differences in response to atomoxetine in children and adolescents; (2) if differences exist as to the time to response of atomoxetine between children and adolescence; and (3) if differences exist as to tolerability of atomoxetine in children and adolescents.

Summary:

**Objective:** Controversy exists as to the tolerability and response of medications in Attention-Deficit/Hyperactivity Disorder (ADHD) across the lifespan. We now report on data contrasting the efficacy and tolerability of atomoxetine between children and adolescents with ADHD.

**Method:** Data from adolescents (122 atomoxetine, 69 placebo) and children (539 atomoxetine, 341 placebo) with DSM-IV ADHD enrolled in similarly designed, double-blind, placebo-controlled trials were analyzed. Efficacy measures included mean change-from-baseline-to-endpoint in the ADHD Rating Scale (ADHD RS), Conners’ Parent Rating Scale and Clinical Global Impressions, remission rate (total ADHD RS T-score ≤ 60 at endpoint) and time-to-remission.

**Results:** Adolescents had lower overall ADHD scores at baseline compared to children. There were no statistically significant differences in the overall effects on ADHD symptoms, remission rates, or the time to remission between age groups. Adverse events were clinically minor and there were no clinically meaningful treatment differences on vital signs, weight, height, lab values, or ECG between children and adolescents.

**Conclusion:** Acute atomoxetine treatment appears to be equally effective and tolerated in children and adolescents with ADHD. These findings refute the notion of pharmacological differences in response to ADHD in children compared to adolescents.

**Funding Source(s):** Funding provided by Eli Lilly and Company.

References:

**NR579** Wednesday, May 5, 12:00 p.m.-2:00 p.m.
**Longer-Term Treatment With Atomoxetine in Adolescents With ADHD**
Supported by Eli Lilly and Company

Timothy E. Wilens, M.D., Department of Child Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC 725, Boston, MA 02114; Jeffrey H. Newcorn, M.D., Christopher J. Kratochvil, M.D., Douglas L. Gelowitz, Ph.D., Christine Thomason, Ph.D., Haitao Gao, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the attendee should have an increased awareness of the effectiveness, safety, and tolerability of atomoxetine in adolescents treated openly for up to two years.

Summary:

**Objective:** There is a paucity of longer-term studies of ADHD, particularly in adolescents. We now report on the effectiveness, safety, and tolerability of atomoxetine (ATMX) in adolescents treated openly for up to two years.

**Methods:** Data from 12 to 18 year-old adolescents with DSM-IV-defined ADHD enrolled in similarly designed clinical trials of ATMX were pooled. Primary efficacy was analyzed using the ADHD Rating Scale (RS) based on parent reports and safety/tolerability from measurement of vital signs, growth parameters, ECG, and laboratories conducted throughout the study.

**Results:** 414 subjects were treated for ≥1 year; 218 (53%) completed greater than two years of treatment at the time of analysis. The mean modal dose (±SD) of ATMX was 1.46 mg/kg/day (0.33). Mean ADHD RS total scores were significantly improved at endpoint compared to baseline (p<.001); scores improved significantly over the first 3 months and remained improved up to 24 months. Adolescents discontinued the trial for reasons including lack of efficacy (N=31, 7.5%) and adverse events (N=11, 2.7%). There were no clinically meaningful effects seen in laboratory values, vital signs, height and weight, or ECG.

**Conclusions:** ATMX remained efficacious during the two-year open trial and does not appear to be associated with the development of new or unexpected safety concerns.

**Funding Source(s):** Funding provided by Eli Lilly and Company.

References:
Educational Objectives:

The purpose of the study was to investigate the link between duration of untreated psychosis and clinical outcome in first-episode psychosis.

Summary:

Objectives: The purpose of the study was to investigate the relationship between duration of untreated psychosis (DUP) and the clinical outcome of first-episode schizophrenia in Korea.

Methods: The charts of the first-episode of schizophrenia and the follow-up period over at least three years for DSM-IV were reviewed. DUP was defined as the interval between the onset of psychotic symptoms (delusions and hallucinations) and the initiation of adequate treatment. Data were collected from the final 27 patients who could be assessed during the follow-up period on a number of predictor variables and outcome variables.

Results: Mean follow-up period was 51.7 months (S.D.=±42.9). Mean DUP was 269.6 days (S.D.=±43708). Long DUP lead to long-term hospitalization. In longer DUP group, respective PANSS-score was higher, although these results wasn’t statistically significant.

Conclusions: This study highly suggests that long DUP can predict poor outcome, such as long-term hospitalization and follow-up PANSS scores, in first-episode schizophrenia.

References:


NR581 Wednesday, May 5, 12:00 p.m.-2:00 p.m.

Quality of Life in First-Episode Psychosis
Ingrid Melle, M.D., Department of Psychiatry, Ulleval Hospital, Kirkeveien 166, Oslo N0407, Norway, Ulik Haahr, M.D., Svein Friis, M.D., Tor K. Larsen, M.D., Per Vaglum, M.D., Jan J. Roessberg, M.D., Thomas H. McGlashan, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize central issues regarding the clinical importance and measurement of quality of life for first episode patients.

Summary:

Background: Quality of life (QoL) is a central issue in the study of psychotic disorders, but few studies have evaluated QoL in first episode patients (FEP). How well do instruments developed for chronic patients apply to FEP, how does FEP describe their subjective QoL and clinical status in the early treatment phase?

Material and method: The TIPS study included consecutive FEP patients. The Lehman Quality of Life Interview (L-QoLI) was measured with the Lehman Quality of Life Interview (L-QoLI). At start of treatment, 262 patients completed full L-QoLI interviews. DUP was defined as the interval between the onset of psychotic symptoms (delusions and hallucinations) and the initiation of adequate treatment. Data were collected from the final 27 patients who could be assessed during the follow-up period on a number of predictor variables and outcome variables.

Results: Mean follow-up period was 51.7 months (S.D.=±42.9). Mean DUP was 269.6 days (S.D.=±43708). Long DUP lead to long-term hospitalization. In longer DUP group, respective PANSS-score was higher, although these results wasn’t statistically significant.

Conclusions: This study highly suggests that long DUP can predict poor outcome, such as long-term hospitalization and follow-up PANSS scores, in first-episode schizophrenia.

References:


NR582 Wednesday, May 5, 12:00 p.m.-2:00 p.m.

Brain-Derived Neurotrophic Factor Measurement in Serum of Schizophrenia
So Youn Kim, M.D., Psychiatry Department, Chungang University Medical School, Hamgagamro3ga65-207 Youngsamgu, Seoul 140–757, Korea; Baik Seek Kee, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to demonstrate neurodevelopmental activity of neurotrophic factors that may contribute the etiology or pathology of schizophrenia.

Summary:

Objectives: Neurotrophic factors regulate neuronal development as well as synaptic plasticity, and their impairment is often implicated as a cause of schizophrenia. Among various neurotrophic molecules, brain-derived neurotrophic factor (BDNF) levels have been found to be increased in the corticolimbic regions of patient’s brains. BDNF, a 23 kDa protein and a member of the neurotrophin family, plays important roles in the survival, growth and maintain of neuronal and glial cells as well as some non-neuronal tissues.

Methods: We assessed peripheral BDNF levels in the serum of two groups of schizophrenia (m=49) and healthy volunteers (m=50). BDNF protein levels in fresh serum of patients and volunteers were measured using a ELISA kit (BDNF Emax immunoassay system, promega Co. USA) and severity of psychotic symptom was evaluated with PANSS.

Results: BDNF levels were significantly increased in the serum of schizophrenia patients (22.40 ± 14.40 vs 36.29 ± 19.78 mg/ml, Mann-Whitney V test, P=0.0007). Abnormal levels of BDNF are evident not only in the brain of schizophrenia patients, but also in their peripheral blood. The direction of BDNF change in serum was proportional to that observed in the brain of schizophrenic patients.

Conclusion: This results suggest that schizophrenia is characterized by high serum BDNF levels and support the hypothesis of neurotrophic factor involvement in psychotic disorder.

References:


NR583 Wednesday, May 5, 12:00 p.m.-2:00 p.m.

The Relationship Between Cognitive Measures and Functional Outcomes in Schizophrenia
Supported by Janssen Pharmaceutica and Research Foundation
Gahan J. Pandina, Ph.D., Medical Affairs Department, Janssen Pharmaceutica, Inc., 1125 Trenton-Harbourton Road, Titusville, NJ 08560; Georges Gharabawi, M.D., Stephen Rodriguez, M.S., Robert Lasser, M.D.
Educational Objectives:
At the conclusion of this session, the participant will better understand the relationship between cognitive measures and functional outcomes in schizophrenic patients treated with long-acting, injectable risperidone.

Summary:
Objective: To examine the relationship between cognitive measures and functional outcomes in schizophrenic patients treated with long-acting, injectable risperidone.
Methods: Data were derived from an ongoing, randomized, double-blind, 52-week, prospective study of 324 stable patients with schizophrenia/schizoaffective disorder receiving 25 or 50 mg of risperidone every two weeks. Measures of cognition, functioning, quality of life, and efficacy were assessed. Interim data on measures of cognition are currently available. Additional interim data, including preliminary analyses of functional and clinical outcomes, will be available for the meeting.
Results: Initial data (n = 60) at 6 months showed significant improvements in a range of cognitive functions: simple motor speed (finger tapping test total taps, right mean = 11.3, P<0.05), attention (continuous performance test flanker version sum correct neutral mean = 3.3, P=0.05), executive functioning (strategic target detection test: target reaction time mean = -174.7 msec, P<0.01; total errors mean = -12.7, P<0.02; nonperseverative errors mean = -9.7, P<0.01), and verbal memory (working list memory total trial 1, mean = 0.8, P<0.03; total learning mean = 5.7, P<0.02). These results will be correlated with measures of social cognition, efficacy, and functioning.
Conclusion: The results suggest that cognitive improvements can occur in stable, schizophrenic patients treated with long-acting risperidone.

Supported by Janssen Pharmaceutica Products, L.P.

References:

NR584  Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Metabolic Syndrome in Patients With Schizophrenia
Supported by Janssen Pharmaceutica and Research Foundation
Gahan J. Pandina, Ph.D., Medical Affairs Department, Janssen Pharmaceutica, Inc., 1125 Trenton-Harbourton Road, Titusville, NJ 08560; Andrew Greenspan, M.D., Cynthia Bossie, Ph.D., Ibrahim Turkoz, M.S., Jacqueline Morein, Jonathan M. Meyer, M.D.

Educational Objectives:
At the conclusion of this session, the participant will better understand the prevalence of metabolic syndrome in patients with schizophrenia and schizoaffective disorder.

Summary:
Background: The metabolic syndrome is a recognized risk factor for cardiovascular disease, but limited data exist regarding the prevalence among patients with schizophrenia compared to the general population.
Objective: To examine the prevalence of metabolic syndrome in patients with schizophrenia.
Methods: The prevalence of the metabolic syndrome at baseline (according to National Cholesterol Education Program guidelines) was assessed in 121 patients with schizophrenia or schizoaffective disorder, intolerant of, or poorly responding to ≥30 days’ treatment with olanzapine, enrolled in a 6-week, open-label, rater-blinded risperidone switch study.
Results: Of the 121 patients, 65 (54%) had metabolic syndrome at baseline, compared to a US national prevalence of 24%. Patients with metabolic syndrome had significantly higher body mass index (35.9 ± 5.1 vs 31.6 ± 8.0; P<0.01). There was no significant between-group difference in age, (P=0.45; mean ± SD, 41.1 ± 10.2 years, sex (P=0.78; 50.4% male), baseline dose of olanzapine (P=0.26; mean ± SD, 15.6 ± 6.7 mg/day), or illness duration (P=0.41; 76.0% of patients diagnosed ≥5 years prior to baseline), although Caucasian ethnicity was more strongly associated with having metabolic syndrome than nonwhite ethnicity (P=0.042).
Conclusions: Results suggest that the metabolic syndrome is highly prevalent among obese patients with schizophrenia/schizoaffective disorder when carefully screened, and represents another long-term risk for cardiovascular disease.

Supported by Janssen Pharmaceutica Products, L.P.

References:

NR585  Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Sexual Dysfunction in Schizophrenia
Supported by Bristol-Meyers-Squibb
Mark Olsson, M.D., Department of Psychiatry, Columbia University, 1051 Riverside Drive, Box 24, New York, NY 10032; Eskinder Tafesse, Ph.D., William H. Carson, Jr., M.D., Steven Connolly, Christopher Guardino

Educational Objectives:
At the conclusion of this session, the participant should be able to describe the frequency and clinical correlates of sexual dysfunction in antipsychotic-treated outpatients with schizophrenia.

Summary:
Background: Although sexual dysfunction is common in antipsychotic-treated male outpatients with schizophrenia, little is known about its clinical consequences.
Methods: A systematic sample of 144 male outpatients with schizophrenia or schizoaffective disorder, aged 18 to 70, treated with antipsychotic monotherapy (haloperidol, olanzapine, risperidone, or quetiapine) for at least six weeks, but not on other medications known to cause sexual side-effects, were assessed with the Changes in Sexual Function Questionnaire (CSFQ), Quality of Life-Interview (QLI), Brief Psychiatric Rating Scale (BPRS), Calgary Depression Scale (CDS), and Global Assessment Scale (GAS).
Results: Current sexual dysfunction was reported by 45.5% of the study patients. The rate of sexual dysfunction was similar in patients treated with quetiapine (40.0%), haloperidol (41.8%), risperidone (53.3%), and olanzapine (59.0%). As compared with patients without sexual dysfunction, those with sexual dysfunction reported significantly poorer quality of life in general (p<0.02) and less satisfaction with the amount of enjoyment in their lives (p=0.04). They were also significantly less likely to have a romantic partner (16.4% vs 39.7%, p=0.003), though not less likely to be married (6.8% vs 8.2%, p=0.72). Patients with and without sexual dysfunction had significantly lower social satisfaction scores (p<0.05).

Supported by Bristol-Meyers-Squibb

References:
dysfunction did not significantly differ in overall symptom severity (mean BPRS: 46.0 vs 43.3), severity of depressive symptoms (mean CDS: 2.7 vs 2.5), or global function (mean GAS: 46.0 vs 43.3).

Conclusions: Sexual dysfunction is common in male patients treated with haloperidol, olanzapine, risperidone, orquetiapine and is associated with impaired self-reported quality of life. Psychiatrists should routinely monitor male patients for sexual dysfunction and consider therapies with less evidence of sexual side-effects.

Funding Source(s): Bristol Myers Squibb Company.

References:

NR586 Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Atypical Antipsychotics and Receptor Binding: Enhancing Cognition and Mood Supported by Pfizer Inc.

Darius Shayegan, B.S., Neuroscience Education Institute, 5857 Owens Avenue, #102, Carlsbad, CA 92008; Stephen M. Stahl, M.D.

Educational Objectives:
At the conclusion of this session, the participant should understand the receptor binding actions for each of the five atypical antipsychotics and discuss the theoretical implications this has for efficacy in improving cognition and mood in schizophrenia.

Summary:
Objective: Schizophrenia is characterized by a diversity of symptoms that hypothetically arise from heterogeneous neuroanatomical and neurochemical malfunctions. This review will profile the unique portfolio of receptor binding actions for each of the five first-line atypical antipsychotics (risperidone, olanzapine, quetiapine, ziprasidone, and aripiprazole) and discuss the theoretical implications these binding properties hold for potential efficacy in improving cognition and mood in schizophrenia.

Methods: Articles characterizing receptor binding properties of atypical antipsychotics were selected by means of search in MEDLINE.

Results: All antipsychotic agents target the key hypothalamic neurotransmitter in psychosis-excessive dopamine neurotransmission at dopamine-D2 receptors in the mesolimbic pathway of the brain—presumably responsible for the positive symptoms of schizophrenia. All atypical antipsychotic agents are serotonin-2A (5-HT2A)/dopamine-D2 antagonists or D2 partial agonists, properties that contribute to reduced motor side effects. Interaction with 5-HT2C, 5-HT1D and 5HT1A receptors, and serotonin and norepinephrine reuptake sites, in human brain tissue predict cognitive improvement, heightened negative symptom relief, and enhanced modulation of mood. Affinity for al-adrenergic receptors, histamine H1 receptors and muscarinic M1 receptors predicts orthostatic hypotension, sedation, cognitive disturbance or weight gain.

Conclusions: Receptor binding properties other than serotonin-2A/dopamine-D2 occupancy may explain cognitive and affective symptom improvement associated with atypical antipsychotic therapy.

Funding Source(s): Pfizer, Inc.

References:

NR587 Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Atypical Antipsychotics and Health Care Costs in VA Patients With Schizophrenia Supported by Eli Lilly and Company

Wei Yu, Ph.D., VA Palo Alto Healthcare System, 795 Willow Road, Menlo Park, CA 94025; Yu-Hui Huang, M.P.H., Steve Ren, Ph.D., Austin Lee, Ph.D., Lewis Kazis, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize the differences in healthcare utilization and costs prior to and post initiation of olanzapine versus risperidone among high-utilization patients diagnosed with schizophrenia.

Summary:
Hypothesis: Effects of olanzapine and risperidone on healthcare costs are different among high-utilization patients with schizophrenia.

Methods: We identified patients whose 12-month cost prior to initiation of the target drugs was in the 95th percentile (n=925) in the Veterans Affairs (VA) system. We examined subsequent one-year differences in costs between Olanzapine and Risperidone, using six categories of healthcare utilization (Inpatient; medical/surgical, psychiatric, and other; Outpatient: psychiatric, other, and antipsychotics).

Results: Prior to initiation, the average 12-month cost was around $110,000; inpatient cared accounted for about 80% of the total. Olanzapine initiators had higher cost for inpatient psychiatric care ($72,222 vs $60,207; p<0.05) and lower cost for inpatient medical/surgical care ($14,366 vs $21,654; p<0.05) than Risperidone initiators. During the 12 months post initiation, the average costs reduced by almost 50% for both drugs. Olanzapine initiators showed greater reduction in inpatient psychiatric costs ($37,278 vs $31,016 p<0.001) but smaller reduction in inpatient medical/surgical costs ($8,644 vs $14,960; p<0.001) than Risperidone initiators. However, the overall cost reductions between Olanzapine and Risperidone initiators were not statistically different from each other.

Conclusion: Among high utilizers, while Olanzapine and Risperidone achieved similar overall cost reductions, the patterns of utilization differ between the two target drugs.

Funding Source(s): Eli Lilly and Company.

References:

NR588 Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Risk of Rehospitalization: Olanzapine Versus Quetiapine Supported by Eli Lilly and Company

Peter F. Wang, M.D., Pharma Research, Premier Healthcare, 2320 Cascade Point Boulevard, Charlotte, NC 28266;
Zhongyun Zhao, Ph.D., Liesl Cooper, Ph.D., Barbara L. Gaylord, M.B.A., Benjamin Gutierrez, Ph.D.

**Educational Objectives:**

At the conclusion of the presentation, participants should gain a better understanding of the differential impact of atypical antipsychotic treatment on rehospitalization for individuals with schizophrenia.

**Summary:**

**Objective:** To compare rehospitalization rates of individuals with schizophrenia who had been treated and discharged on olanzapine or quetiapine from acute care hospitals.

**Methods:** Using Premier's Perspective TM database, the largest U.S. hospital drug utilization database, rehospitalization status for inpatients with schizophrenia (ICD-9-CM: 295.xx), who were successfully treated and discharged on olanzapine (N=7,573) or quetiapine (N=3,368) between 01/1999 and 09/2001. A successful treated patient was one who started treatment with olanzapine or quetiapine in hospital and discharged on the same antipsychotic. Time to readmission up to 33 months was analyzed by Kaplan-Meier models. Cox proportional hazard models were used to derive the hazard ratio (HR) for rehospitalization by adjusting potential confounding factors.

**Results:** Overall rehospitalization rate in the study population was 35.3%. After adjusting for potential confounding factors, quetiapine therapy (average daily dose=356.1 mg) was associated with a 25% increased risk of rehospitalization compared to olanzapine (average daily dose=17.3 mg) (HR=1.25, 95% confidence interval 1.17–1.34, p<0.0001). Additionally, younger age, schizoaffective/paranoid diagnoses, higher severity level, and urban hospital location were significantly associated with a higher risk of readmission.

**Conclusions:** This study suggests that olanzapine-treated patients had lower risk of rehospitalization than quetiapine-treated patients. Moreover, certain patient demographic/clinical factors and institution characteristics also influenced hospital readmission. Funded by Eli Lilly and Company

**References:**


**NR589** Wednesday, May 5, 12:00 p.m.-2:00 p.m.

**Comparison of Quetiapine Versus Risperidone in Treating Negative Symptoms Supported by AstraZeneca Pharmaceuticals**

Michael Riedel, M.D., Department of Psychiatry, Munich University Hospital, mussbaumstrasse 7, Munich 80366, Germany; Hans-Jurgen Moller, M.D., Martin Strassnig, M.D., Ilja Spellmann, M.D., Anette Muller-Arends, M.D., Sanora Dehning, M.D., Nikolai Sandowsky, M.D., Norbert Muller, Ph.D.

**Educational Objectives:**

At the conclusion of this session, the participant should be able to: (1) compare the efficacy of quetiapine and risperidone in patients with predominantly negative symptoms; (2) provide further data on the tolerability of those two atypical agents.

**Summary:**

**Objective:** Negative symptoms of schizophrenia are associated with relapse, poor social functioning, cognitive impairment, and a lower QoL (1). There have been few direct comparisons between atypical antipsychotics in creating negative symptoms (2). This study compared the efficacy and tolerability of risperidone versus quetiapine (‘Seroquel’).

**Methods:** A 12-week, double-blind comparison of risperidone and quetiapine was conducted in 44 patients with schizophrenia and predominantly negative symptoms. The PANSS and the SANS were used to evaluate efficacy, and the SAS for EPS. Assessments were performed at Weeks 1–8, 10 and 12. Data were analyzed using LOCF and MANOVA.

**Results:** Twenty-five patients completed the study. Both quetiapine (mean dose 574 mg/day) and risperidone (mean dose 4.91 mg/day) produced significant improvements in PANSS total, positive and negative scores, and SANS scores. Quetiapine showed a significant advantage over risperidone in the SANS attention subscale (p<0.05). Patients treated with risperidone had a significantly greater incidence of EPS (p<0.01 at Weeks 3, 4, 5, and 7) and required significantly higher dosages of anticholinergic medications at Weeks 3–8 (p<0.05).

**Conclusions:** Quetiapine and risperidone are equally efficacious against negative symptoms; however, quetiapine also improves attention and is better tolerated, with a lower propensity for EPS and anticholinergic medication requirement.

**Funding Source(s):** AstraZeneca

**References:**


**NR590** Wednesday, May 5, 12:00 p.m.-2:00 p.m.

**Schizophrenia and Weight Management: A Systematic Review of Intervention**

Keith R. Lloyd, M.D., Mental Health Department, Peninsula Medical School, Wonford House, Dryden Road, Exeter EX2 5AF, United Kingdom; Andrew A. Souldy, M.S.C., Guy Faulkner, Ph.D.

**Educational Objectives:**

At the conclusion of this session, the participant should demonstrate a knowledge of effective interventions for weight management in schizophrenia.

**Summary:**

**Objective:** Weight gain is a frequent side effect of anti-psychotic medication, which has serious implications for a patient’s health and well being. This study systematically reviews the literature on the effectiveness of interventions designed to control weight gain in schizophrenia.

**Method:** A systematic search strategy was conducted of major databases in addition to citation searches. Study quality was rated.

**Results:** Sixteen studies met the inclusion criteria. Five of eight pharmacological intervention studies reported small reductions in weight (<5% baseline body weight). All behavioral (including diet and/or exercise) interventions reported small reductions in, or maintenance of, weight.

**Conclusions:** Weight loss may be difficult but it is not impossible. Given the inconsistent results, the widespread use of pharmacological interventions cannot be recommended. Both dietary and exercise counseling set within a behavioural modification programme is necessary for sustained weight control.
NR591  Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Acceptability and Disintegration Rates of Orally Disintegrating Risperidone
Supported by Janssen Pharmacuetica and Research Foundation
Pierre Chue, M.D., Psychiatry Department, CLIP Clinic, 3rd Floor, 9942-108 Street, Edmonton, AB T5K 2J5, Canada; Ron P. Welch, B.S.C.

Educational Objectives:
At the conclusion of this session, the participant should be able to identify situations where rapid dissolving formulations of atypical antipsychotics are of value and recognize the utility of the rapid dissolving dosage form in the treatment of the mentally ill, especially when compliance problems are manifest.

Summary:
Objective: The rapid dissolving formulations of the atypical antipsychotics provide clinicians with a therapeutic option that improves compliance in various treatment settings. We investigated the disintegration profile, acceptability and tolerability of orally disintegrating risperidone tablets in subjects with schizophrenia and schizoaffective disorder.

Methods: Ten subjects stable on monotherapy with once daily risperidone 2mg to 4mg were switched to an equivalent dose of orally disintegrating risperidone for seven days. Visual assessments for time to initial and complete disintegration were collected at each visit. Clinical Global Impression Severity scores (CGI-S) were collected at baseline and at last visit. Subject acceptance of the new formulation was obtained at last visit on a visual analog scale.

Results: Subjects maintained their stable clinical status. Mean time to initial disintegration was 5.1 sec (SD=0.8) and mean time to complete disintegration was 29.4 sec (SD=18.4). Mean acceptability rating was 9.61 (SD=0.61). Adverse events were reported by 5 patients and were mild in severity.

Conclusion: The exceptional dissolution, portability and high subject acceptance of risperidone rapid dissolving tablets will provide a valuable option in the treatment of the noncompliant patient.

Funding Source(s): Funding provided by Janssen Pharmaceuticals Canada

References:

NR592  Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Investigation of the Metabolic Effects of Antipsychotics in Schizophrenia Patients
Supported by Janssen Pharmaceuticals Canada
Pierre Chue, M.D., Psychiatry Department, CLIP Clinic, 3rd Floor, 9942-108 Street, Edmonton, AB T5K 2J5, Canada; Ron P. Welch, B.S.C., John C. Lind, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to: (1) recognize that antipsychotic medications predispose to metabolic dysregulation; (2) that the mechanism is poorly understood, but multifactorial; and (3) to incorporate the differential liability amongst agents into assessment and treatment.

Summary:
Objective: To prospectively examine the metabolic effects of conventional (CAPs) and atypical (AAPs) antipsychotics in patients with a DSM-IV diagnosis of schizophrenia. The objective of this study was to identify patients with metabolic syndrome (metabolic syndrome). The metabolic syndrome is a precursor for the development of coronary heart disease and diabetes mellitus. Studies have shown that waist measurement, a measure of central obesity, may be a simple way to initially identify patients with metabolic syndrome. In this pilot study we determine if waist circumference can identify schizophrenic patients at risk of having metabolic syndrome.

Method: Cross-sectional study of 31 female and 32 male patients recruited from an outpatient psychiatric clinic. Metabolic syndrome was defined using the ATP III criteria.

Results: Sixty-seven per cent of patients had a waist measurement identifying central obesity. Metabolic syndrome was present...
in 79% of patients with central obesity and in 19% of patients with normal waist (p < .001). Pearson correlations showed an association of waist circumference with high-density lipoprotein (r=−0.31, p<.05), systolic blood pressure (r=0.36, p<.01), and diastolic blood pressure (r=0.44, p<.001). In multiple regression analyses association between waist circumference and high-density lipoprotein, systolic blood pressure, and diastolic blood pressure remained significant.

**Conclusion:** Data in this report suggest waist circumference is a strong predictor of components of metabolic syndrome. We propose the measurement of waist circumference as a screening tool for metabolic syndrome in this population. It can provide an opportunity for primary prevention of coronary heart disease and diabetes mellitus in patients with schizophrenia. The patients with increased waist circumference should be encouraged to lose weight and increase their physical activity.

**References:**

**NR594 Wednesday, May 5, 12:00 p.m.-2:00 p.m.**

**Use of Multiple Atypical Antipsychotics in Severely and Persistently Mentally Ill Patients**

James L. Megna, M.D., Department of Psychiatry, State University of New York, UMU, 750 E. Adams Street, Syracuse, NY 13210; Arun Raj Kunwar, M.D.

**Educational Objectives:**
At the conclusion of this session, the participant should learn different strategies to treat severely and persistently mentally ill patients.

**Summary:**

**Objective:** To evaluate the safety and efficacy of the combination use of atypical antipsychotics in severely persistently mentally ill (SPMI) individuals.

**Method:** This is a retrospective chart review of the patients who were admitted in a state psychiatric facility and were receiving more than one atypical antipsychotic. This study was conducted from June 1999 through December 1999. Brief Psychiatric Rating Scale (BPRS) score, Clinical Global Impression: Severity (CGI:S) score, number of pm medication administrations, and number of patients receiving anticholinergic medication were compared at baseline and at six months post regimen implementation. The Institutional Review Board approved the study.

**Results:** Out of 124 patients, 24 were prescribed more than one atypical antipsychotics. This group showed 26% improvement in BPRS symptoms from baseline to 6 month which was statistically significant (34.2 ± 11.0 vs 25.3 ± 11.8; P=0.016). CGI:S also showed improvement from baseline of 5.5 ± 0.6 to 5.0 ± 0.8 (P=0.016). Average number of PRN medication administrations also fell from 7.6 ± 19.6 to 1.6 ± 2.6 (P=0.04) and there was increase in number of patients receiving anticholinergic medication from 5 to 8 (P=0.04).

**Conclusions:** Use of more than one atypical antipsychotic may be beneficial in treatment of SPMI individuals.

**References:**
Long-Term Impact of Olanzapine and Risperidone on Sexual Dysfunction
Supported by Eli Lilly and Company

Haya Ascher-Svanum, Ph.D., Department of Outcomes Research, Eli Lilly, Lilly Corporate Center, Indianapolis, IN 46285; Baojin Zhu, Ph.D., Douglas E. Faries, Ph.D., Qin Jiang, M.S., Bruce J. Kinon, M.D.

Educational Objectives:
At the conclusion of this session, participants will be able to recognize that minimizing sexual dysfunction related to treatment of schizophrenia may improve emotional well-being, life satisfaction, and adherence with medications.

Summary:
Objectives: To compare olanzapine and risperidone on reported sexual dysfunction during the long-term treatment of schizophrenia patients in usual care, and to examine the associations between sexual dysfunction, medication adherence, and indicators of well-being for all patients.

Method: Data of the U.S. Schizophrenia Care and Assessment Program (SCAP), a 3-year observational study of schizophrenia, were used to identify olanzapine (N=372) and risperidone (N=229) treated-patients at enrollment who continued on the drug for at least one year. The SCAP-Health Questionnaire measured patient-reported medication-related sexual dysfunction at six-month intervals. Changes in sexual dysfunction levels from baseline up to three years were examined using a mixed model with repeated measures. Pearson correlations examined associations between sexual dysfunction, medication adherence and indicators of well-being at enrollment.

Results: Compared with risperidone-treated patients, those treated with olanzapine reported significantly greater long-term improvements in medication-related sexual dysfunction (p<0.001). Greater sexual dysfunction was significantly (p<0.05) associated with greater emotional distress, poorer mental functioning, lower life satisfaction, less satisfaction with social life, and poorer self-reported medication adherence.

Conclusion: Treatment with risperidone was associated with greater sexual dysfunction compared to olanzapine. Findings suggest that minimizing treatment-related sexual dysfunction may decrease emotional distress, improve life satisfaction, and increase adherence with medication.

Funded by Eli Lilly and Company

References:

NR598 Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Long-Term Cognitive Improvement in Patients Switched to Ziprasidone
Supported by Pfizer Inc.

Antony D. Loebel, M.D., Pfizer Inc, 235 East 42nd Street, 8th Floor, New York, NY 10029; Philip D. Harvey, Ph.D., Stephen R. Murray, M.D., Evan Batzar, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participant should gain an improved understanding of antipsychotic-related improvement in cognitive function and its implications for functional outcome, with specific reference to changes in cognitive test performance in patients receiving long-term treatment with ziprasidone.

Summary:
Objective: Memory impairment in schizophrenia is associated with functional impairment. We examined improvement in memory functions associated with ziprasidone in patients switched from other antipsychotics.

Methods: Three open-label, flexible-dose continuation studies enrolled patients who completed 6-week trials wherein they had been switched to ziprasidone from conventional antipsychotics, risperidone, or olanzapine due to suboptimal antipsychotic efficacy or tolerability. Learning and memory were assessed at last visit with the Rey Auditory Verbal Learning Test (RAVLT). Changes from the core study baseline to endpoint in the ITT population are reported.

Results: Overall, median treatment duration was 215 days. Patients in all three studies demonstrated significant improvement in multiple components of the RAVLT. Patients switched from conventional antipsychotics (n=71) demonstrated improvement in performance on first learning trial (P<0.001), Total Learning over
five learning trials (P<0.05), and Long Delay Recall (P<0.05) components. Patients switched from olanzapine (n=71) exhibited improvement in Trial One Performance (P<0.0005), Total Learning (P<0.0001), and Long Delay Recall (P<0.005). Patients switched from risperidone (n=43) improved significantly on Total Learning (P<0.05) and Long Delay Recall (P<0.01).

Conclusions: Patients switched to ziprasidone may experience improvement in learning and memory over a longterm period. The functional consequences of the improvements are yet to be determined.

Supported by funding from Pfizer Inc.

References:

NR599 Wednesday, May 5, 12:00 p.m.-2:00 p.m.
BMI Glucose Levels in Patients With Schizophrenia Before and After Aripiprazole
Supported by Bristol-Myers-Squibb
Robert E. Litman, M.D., Centers for Behavioral Psychiatry, 14915 Broschart Road #250, Rockville, MD 20850; Megan Miaoarca, R.N., Elizabeth Courage, B.S., Carlos Collin, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be more informed with regard to metabolic side effects of atypical antipsychotic treatments, focusing on olanzapine and aripiprazole; clinical rationale, benefit and risks of switching antipsychotic therapies in otherwise stable patients.

Summary:
Objective: To determine the effect of switching from chronic olanzapine therapy to aripiprazole therapy on body mass indices, lipids, and glucose metabolism in schizophrenia patients.
Methods: Fasting and 2-hr postprandial plasma glucose, plasma lipids, and BMI were measured in nine physically healthy patients with schizophrenia or schizoaffective disorder on chronic olanzapine therapy and then again after patients were on stable doses of aripiprazole for 12 weeks. Measures on olanzapine therapy were compared with measures on aripiprazole therapy utilizing Wilcoxon Signed Ranks Test.
Results: Compared with olanzapine, aripiprazole-treated patients had significant reductions in BMI (31.7 kg/m² vs 30.5 kg/m²; p<.02) and cholesterol (233.7 mg/dl vs. 194.6 mg/dl; p<.02). Although differences in other metabolic indices did not reach statistical significance, they were substantial and clinically significant for triglyceride levels in three of nine patients and for response to glucose challenge in three of eight patients. No significant changes in HbA1c were observed.
Conclusions: These preliminary data suggest the possibility that switching to aripiprazole from olanzapine may improve BMI and cholesterol levels. While improvement in other metabolic indices was also seen in individual patients, establishing generalizability of these findings will require further investigation in a larger patient sample.

References:

NR600 Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Ziprasidone Versus Haloperidol Treatment of Agitation
Supported by Pfizer Inc.
Leslie L. Citrome, M.D., Nathan Kline Institute, 140 Old Orangeburg Road, Building 37, Orangeburg, NY 10962; Shlisho Brook, M.D., Lewis Warrington, Ph.D., Antony D. Loebel, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to compare the utility of sequential IM/oral ziprasidone versus IM/oral haloperidol in the treatment of hostile and excitable patients with schizophrenia or schizoaffective disorder.

Summary:
Objective: To compare the efficacy of sequential IM/oral ziprasidone vs IM/oral haloperidol in the treatment of hostility and excitability in patients with acute schizophrenia or schizoaffective disorder.
Methods: Post hoc analyses of pooled data from two studies comparing mean reductions in BPRS hostility, agitation, and excitability item scores over the first seven days. In the first study (a 7-day study), 90 patients received ≤3 days IM ziprasidone, then oral ziprasidone (80–200 mg/d, mean 90.5 ± 44.9 mg/d) and 42 patients received IM haloperidol, then oral haloperidol (10–80 mg/d, mean 14.0 ± 10.1 mg/d). In the second study (a six-week study), 417 patients received IM ziprasidone, then oral ziprasidone (80–160 mg/d, mean 116 ± 30.4 mg/d) and 133 patients received IM haloperidol, then oral haloperidol (5–20 mg/d, mean 11.5 ± 3.6 mg/d).
Results: Overall, patients demonstrated improvement on the hostility (p=0.004) and agitation (p=0.0001) items of the BPRS. Ziprasidone was more effective than haloperidol on the excitability (p=0.02) and agitation (p=0.01) items.
Conclusions: Ziprasidone was superior to haloperidol in the treatment of excitability and agitation.
Supported by funding from Pfizer Inc

References:

NR601 Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Psychiatric and Metabolic Outcomes of Antipsychotics in Schizophrenia
Supported by Pfizer Inc.
Sonja V. Sorensen, M.P.H., Medtap International, 7101 Wisconsin Avenue, Suite 600, Bethesda, MD 20814; David J. Harrison, Ph.D., Megan C. Leaderer, M.P.H., Manishi Prasad, M.P.H., Christopher S. Hollebeak, Ph.D., Ashish Dugar, Ph.D., Edit Remak, M.S.C.

Educational Objectives:
At the conclusion of this session, the participant will understand the microsimulation approach to modeling and long-term adverse outcomes of atypical antipsychotics in schizophrenia (type 2 dia-
Results: Insulin resistance was improved in 70% of patients. There was a statistically significant difference in baseline and interim HOMA-IR scores (p = .04). Additionally, there were statistically significant improvements in triglycerides (p = .03) and weight (p = .02), with a mean weight loss of 6.59 lbs.

Conclusions: The preliminary results of this pilot study suggest that aripiprazole has a positive effect on insulin resistance and possibly other metabolic abnormalities in schizophrenia patients. These positive effects may further improve with continued treatment with aripiprazole. Further investigation is warranted with larger, controlled trials over a longer period of time.

References:

NR603 Wednesday, May 5, 12:00 p.m.-2:00 p.m.
A Naturalistic Trial With Aripiprazole in a General Psychiatric Setting
Supported by Bristol-Meyers-Squibb and Otsuka Pharmaceutical Co., Ltd
Rajiv Tandon, M.D., Department of Psychiatry, University of Michigan Health System, 1500 East Medical Center Drive, Ann Arbor, MI 48109-0120; Elyse G. Stock, M.D., Linda Riera, B.A., Mary J. Kujawa, M.D., Shirley Lam, Pharm. D., Miranda Pans, M.S.C., Taro Iwamoto, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to understand the overall effectiveness of aripiprazole in patients with schizophrenia.

Summary:
Objective: To demonstrate the overall effectiveness of aripiprazole in a naturalistic setting.

Methods: A multicenter, open-label study of aripiprazole was conducted in patients with schizophrenia or schizoaffective disorder for whom a switch or initiation of antipsychotic medication was needed. Patients were randomized to aripiprazole (n=1295) or a safety-control group (primarily risperidone, olanzapine, ziprasidone, or quetiapine; n=304) for 8 weeks in a 4:1 ratio. The initial dose of aripiprazole was 15mg with option to adjust within a range of 10–30 mg/day. The key effectiveness measures included the CGI-Improvement scale (CGI-I) and preference of medication scale (POMS).

Results: The mean aripiprazole dose at endpoint was 19.9 mg/day with 47% of patients on the 15mg dose. The effectiveness of aripiprazole was demonstrated as early as week 1. In patients completing the study, 69% of patients in the aripiprazole group responded to treatment (CGI-I score of 1 or 2) with a mean CGI-I score of 2.17. Over 60% of aripiprazole-treated patients and 54% of caregivers rated aripiprazole as much better than prior antipsychotic (score of 1). The only adverse events reported with aripiprazole (≥10%) were nausea (14%), and insomnia (20%).

Conclusions: Aripiprazole demonstrated overall effectiveness in patients with schizophrenia and schizoaffective disorder in a general psychiatric setting.

Funding Source(s): Bristol-Myers Squibb Company and Otsuka Pharmaceutical Co., Ltd

References:

NR604 Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Schizoaffective Disorders: Direct Switch to Long-Acting Risperidone
Supported by Janssen-Cilag GMBH

Stein Opjordsmoen, M.D., Acute Psychiatry, Ullevaal Hospital, Kirkeveien 166, Oslo 1255, Norway; Andreas Mohl, M.D., Kirsten Westly, M.D., Alice Lex, M.D., Dieter Naber, M.D.

Educational Objectives:
After reading this poster, the reader should be informed about a novel treatment matching modality and the quality of the subsequent treatment in stable patients with schizoaffective disorder.

Summary:
Objective: The StoRMI trial investigated maintained efficacy and safety of risperidone long-acting injectable in patients with schizoaffective disorder switched directly from other antipsychotic agents without an oral Risperidone run-in.

Methods: Adult patients stable on their antipsychotic regimen for >= one month were switched to Risperidone long-acting (25 mg. Increased to 37.5 mg or 50 mg, if necessary) injected every 14 days for six months.

Results: Among 119 patients (58 male, 61 female) previous therapy was predominantly atypical antipsychotics and classical depot. Reasons for switching: non-compliance (40%), side effects (36%) and insufficient efficacy (26%). 70% of patients completed the 6 months trial. More patients (13%) were 'not ill' by CGI at six months vs. baseline (4%). There were significant improvements from baseline to endpoint in patient satisfaction and GAP. Improvement >=20% in PANSS score was seen in 36% of patients. Mean scores for total PANSS and all factors according to Marder (positive, negative, disorganized thoughts, hostility/excitement and anxiety/depression) were reduced significantly (p<0.05) from baseline to endpoint. No unexpected side effects were reported. EPS scores improved significantly.

Conclusion: Switching directly to risperidone long-acting injectable was effective in patients with schizoaffective disorder, providing sustained improvements of symptoms in patients considered stable on their previous antipsychotic medication.

Funding Source(s): Janssen-Cilag

References:

NR606 Wednesday, May 5, 12:00 p.m.-2:00 p.m.
An Orally-Disintegrating Tablet Formulation of the Antipsychotic Aripiprazole
Supported by Bristol-Meyers-Squibb and Otsuka Pharmaceutical Co., Ltd

David Boulton, Ph.D., Clinical Discovery, Bristol-Myers Squibb, Route 206, Province Line Road, Princeton, NJ 08543; Donna Dressler, B.S., Georgia Kullia, Ph.D., Nimish Vachharajani, Ph.D., Suresh Mallikarjun, Ph.D., William H. Carson, Jr., M.D., David Kornhauser, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to understand that the orally disintegrating tablet (ODT) of aripiprazole offers a convenient and rapid drug delivery system.

Summary:
Objective: To establish bioequivalence of aripiprazole when administered as an orally disintegrating tablet (ODT) compared to the oral tablet.

Methods: Two open-label, randomized, three-period, two-treatment, crossover studies were conducted in healthy subjects to assess the bioequivalence of the ODT relative to the oral tablet at doses of 5 mg (n=38) and 30 mg (n=36). Serial blood samples
were collected for up to 384 h. Bioequivalence was to be concluded if the 90% confidence intervals for the ratio of adjusted geometric means of the ODT to oral tablet were within 80 to 125% for aripiprazole Cmax and AUC(INF).

Results: Both aripiprazole Cmax and AUC(INF) met the criterion for bioequivalence at both doses, with point estimates and 90% confidence intervals for the ratios of the aripiprazole ODT to oral tablet adjusted geometric means of 1.02 (0.96, 1.08) for Cmax and 1.00 (0.96, 1.04) for AUC(INF) at the 5 mg doses, and 1.03 (0.95, 1.12) for Cmax, and 1.01 (0.94, 1.08) for AUC(INF) at the 30 mg doses. Median Tmax, and mean T-half were comparable between the formulations at each dose. No serious adverse events occurred with either formulation at either dose.

Conclusion: The orally disintegrating tablet of aripiprazole was bioequivalent to the oral tablet in healthy subjects with respect to aripiprazole Cmax and AUC(INF), offering a convenient alternative formulation for patients who have difficulty swallowing tablets.

Funding Source(s): Bristol-Myers Squibb Company and Otsuka Pharmaceutical Co., Ltd.

References:


NR607 Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Effect of Antipsychotic Drugs on Diabetes in Schizophrenia: Meta-Analysis
Supported by Bristol-Meyers-Squibb
Gilbert Litalien, Ph.D., Bristol-Myers Squibb, 5 Research Parkway, Wallingford, CT 06492; Klaus Pugner, Ph.D., Jayanti Mukherjee, Ph.D., William Carson, M.D., John W. Newcomer, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant will gain an understanding of the relationship between the use of atypical antipsychotics and the risk for development of new onset diabetes among the major atypicals.

Summary:
Objective: There is growing evidence implicating the newer antipsychotics with diabetes. We conducted a meta-analytic review of the literature to assess this relationship and to provide an evidence-based argument regarding an atypical-diabetes class effect.

Methods: We conducted a comprehensive search of electronic databases (MEDLINE, Current Contents®) for all relevant papers published from January 1, 1990 to November 15, 2002. Studies with at least one atypical treatment for schizophrenia qualified. Summary Odds Ratios (SORs) were computed from reported ORs for three atypicals (clozapine, olanzapine, risperidone) with two referent groups: (1) conventional antipsychotics or (2) no treatment. Mantel-Haenszel fixed-effects models were used to compute weighted SORs.

Results: Of 27 accepted studies, 21 were papers and six were abstracts. SORs for the association between diabetes and clozapine use was 7.44 (95% CI: 1.6-35) versus no treatment and 1.37 (95% CI: 1.1-1.7) versus conventional. For olanzapine use, SORs were 4.02 (95% CI: 1.8-9.6) versus no treatment and 1.37 (95% CI: 1.1-2.1) versus conventional. Risperidone use was not associated with diabetes in either referent category: (1.33[95% CI: 0.6-3.2] versus no treatment and 1.12 [95% CI: 0.8-1.2] versus conventional.

Conclusions: An association between atypical antipsychotic use and incident diabetes appears to be restricted to clozapine and olanzapine, but not risperidone. This evidence suggests that it is premature to ascribe a "class effect" to atypicals.

Funding Source(s): Bristol-Myers Squibb Company

References:


NR608 Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Bioavailability of an Oral Solution of the Antipsychotic Aripiprazole
Supported by Bristol-Meyers-Squibb and Otsuka Pharmaceutical Co., Ltd
Nimish Vachharajani, Ph.D., Clinical Discovery, Bristol-Myers Squibb, Route 206 and Province Line Road, Princeton, NJ 08543; Tracy Vanderslice, M.D., Georgia Kollla, Ph.D., David Boulton, Ph.D., Suresh Mallikaarjun, Ph.D., Taro Iwamoto, Ph.D., David Kornhauser, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to understand the bioavailability of aripiprazole when administered as an oral solution as compared to the tablet.

Summary:
Objective: To estimate the relative bioavailability of aripiprazole when administered as an oral solution as compared to the tablet.

Methods: In two open-label, randomized, crossover studies, aripiprazole was administered in oral solution and tablet formulations to healthy adult subjects as single oral doses of 5, 10, 15, and 30 mg. Serial blood samples were collected for pharmacokinetic assessments up to 384 hours (17 days) post-dose. The bioavailability of aripiprazole from the oral solution as compared to the tablet was determined and the doses of aripiprazole needed to achieve the Cmax and AUC comparable to those from the same tablet dose were estimated. Safety was also monitored throughout the study.

Results: Cmax and AUC satisfied the criterion for dose proportionality for oral solution doses of 5, 10, and 15 mg. At equivalent doses, the peak plasma concentrations of aripiprazole from the solution were higher than the tablets, and the solution systemic exposures were slightly higher than tablets. For 30 mg doses, the oral solution to tablet ratio of geometric mean Cmax values for aripiprazole was 1.22, and that of AUC(INF) was 1.14.

Conclusion: Aripiprazole is well absorbed when administered orally as the solution. The peak and systemic exposures to aripiprazole from oral solution are somewhat greater than those from tablets.

Funding Source: Bristol-Myers Squibb Company and Otsuka Pharmaceutical Co., Ltd

References:


**NR609** Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Investigator's Assessment Questionnaire of Antipsychotics' Effectiveness
Supported by Bristol-Meyers-Squibb

Hong Li, Ph.D., Outcomes Research, Bristol-Myers-Squibb, 5 Research Parkway, Wallingford, CT 06492; Rajiv Tandon, M.D., Jian Han, Ph.D., Gilbert Litalian, Ph.D., Saurabh Ray, Ph.D., William H. Carson, Jr., M.D.

**Educational Objectives:**
By the end of this session, audience should have a good understanding of the Investigator’s Assessment Questionnaire (IAQ) as a new clinical measure of overall effectiveness of antipsychotics and present results of this questionnaire from a clinical trial.

**Summary:**
**Objective:** To describe a new clinical measure of overall effectiveness of antipsychotics in treating schizophrenic patients.

**Methods:** The Investigator's Assessment Questionnaire was used as a secondary measure in an eight-week, randomized, open-label, multicenter study of atypical antipsychotic treatment in 1,520 patients with schizophrenia or schizoaffective disorder. Rated at a five-point Likert scale (1=much improved to 5=much worse), the IAQ is a clinician-administered questionnaire with 12 items that evaluate efficacy, safety, and tolerability when using atypicals to treat schizophrenic patients. A summary score was generated by summing all the item values. Mean total score of the IAQ was used for comparison. Correlation between IAQ and CGI-I and Time to Discontinuation was evaluated.

**Results:** Total IAQ score correlated well with CGI-I score (r=0.81, p<0.0001) and with Time to Discontinuation (r=0.37, p<0.0001). While the mean total score of IAQ of aripiprazole (17.4) was comparable with that of olanzapine (19.9), statistically significant differences (p<0.0001) were found between aripiprazole and ziprasidone (21.5), risperidone (22.4), and quetiapine (22.8).

**Conclusions:** The IAQ is a valid and useful measure of the overall effectiveness of antipsychotics and can be used to differentiate drug effectiveness.

**Funding Source(s):** Bristol-Myers Squibb Company

**References:**

**NR610** Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Metabolic Effects of Combination Antipsychotic and Divalproex Therapy

Dan W. Haupt, M.D., Psychiatry Department, Washington University School of Medicine, 660 South Euclid Avenue, Box 8134, St Louis, MO 63110; Martha Hessler, B.A., Karen S. Flavin, R.N., Julie S. Schweiger, Justin J. Maeda, B.A., Angela Luber, B.S., John W. Newcomer, M.D.

**Educational Objectives:**
At the conclusion of this presentation, the participant should have a broader understanding of efficacy and tolerability issues relating to use of atypical antipsychotics in African-American patients with schizophrenia, with a focus on ziprasidone.

**Summary:**
**Objective:** To better understand the efficacy and tolerability of atypical antipsychotics among ethnic groups, we reviewed data for African-American patients with schizophrenia who participated in clinical trials of oral ziprasidone.
Methods: Efficacy of ziprasidone in African-Americans in short-term (4–6 week), fixed-dose, placebo-controlled (STFDPC) trials was compared with that in Caucasians and the interaction effect of race on efficacy variables explored. Data on tolerability were compiled from patients in these and other short-term (≤12 weeks) trials of ziprasidone.

Results: In STFDPC trials, African-American patients receiving ziprasidone demonstrated greater improvements in PANSST Total, PANSST Negative, BPRS or BPRSD Total, BPRS Core, and CGI-S (n=77 to 99, depending on assessment) than those receiving placebo (n=41 to 66); improvements were comparable to those observed in Caucasian patients (n=255 to 213). Interaction effect (treatment by race) was not significant for any efficacy variables. In STFDPC trials, ziprasidone was well tolerated among African-Americans (n=175), with 4.6% discontinuing due to adverse events. Mean weight gain in African American patients in all short-term trials (n=241) was 1.23 kg, with less weight gain (<0.71 kg) in patients with higher (≥23) BMI.

Conclusions: Ziprasidone is efficacious in African-American patients with schizophrenia and is well tolerated, with minimal weight gain.

Supported by funding from Pfizer Inc.

References:

NR612 Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Intramuscular Aripiprazole in Acutely Agitated Psychotic Patients
Supported by Bristol-Meyers-Squibb and Otsuka Pharmaceutical Co., Ltd

David G. Daniel, M.D., Bioniche Development, PO Box 6207 Mclean, VA 22106, Mclean, VA 22106-7137; Elyse G. Stock, M.D., Charles H. Wilber, M.Ed., Ronald N. Marcus, M.D., William H. Carson, Jr., M.D., George Manos, Ph.D., Taro Iwamoto, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to better understand the effectiveness of intramuscular aripiprazole treatment for acute agitation in patients with psychosis.

Summary:
Objective: To evaluate the efficacy and safety of intramuscular (IM) aripiprazole in the treatment of acute agitation in patients with schizophrenia, schizoaffective, and schizophreniform disorders.

Methods: In a multicenter, 24-hour, double-blind, placebo-controlled study, 357 patients presenting with acute agitation were randomized to placebo, aripiprazole IM doses of 1 mg, 5 mg, 10 mg, and 15 mg, or haloperidol IM 7.5 mg. The key outcome measure was PANSS-Excited Components (PEC), evaluated every 15 minutes for the first 2 hours after dosing.

Results: Aripiprazole 10 mg IM demonstrated rapid reduction of PEC versus placebo (at 30 min: -3.2 vs. -1.76, p = 0.051; 45 min: -4.39 vs. -2.22, p < 0.05; 60 min: -5.48 vs. -2.41, p < 0.05). Efficacy was maintained for the duration of the 24-hour study. Haloperidol exhibited significant improvement versus placebo at 105 minutes. In addition, aripiprazole IM resulted in significant improvement in agitation, without excessive sedation, as measured by the Agitation-Calmness Evaluation Scale. Aripiprazole IM was associated with minimal pain at the injection site (1.8%) and two patients discontinued due to adverse events.

Conclusions: These data suggest that aripiprazole 10 mg IM is an effective treatment for rapid reduction of acute agitation, without excessive sedation or pain at the injection site.

Supported by funding from Pfizer Inc.

References:

NR613 Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Effect of Ziprasidone Initial Dosing on Discontinuation in Schizophrenia
Supported by Pfizer Inc.

Amie T. Joyce, M.P.H., Pharmetrics, 311 Arsenal Street, Watertown, MA 02472-2815; David J. Harrison, Ph.D., Daniel Ollendorf, M.P.H.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to discuss the effect of ziprasidone starting dose on compliance and the database results showing improved medication adherence among patients with schizophrenia who begin ziprasidone therapy with an initial dose of 120–160 mg/day.

Summary:
Objective: To examine the effects of initial ziprasidone dose on discontinuation rates, using the PharMetrics integrated medical and pharmacy claims data.

Methods: Patients ≥18 years with a diagnosis of schizophrenia and a ziprasidone claim between March 2001 and February 2003 continuously enrolled for ≥6 months before and ≥3 months after initiation of ziprasidone were stratified by initial daily dose (≥40 mg and <80mg [low] vs ≥80 mg and <120 mg [medium] vs ≥120 mg [high]). The six-month risk of discontinuation was examined using Cox proportional hazards models controlling for gender, psychiatric comorbidities, and pre-ziprasidone utilization of antipsychotics (atypical, conventional, none).

Results: Mean age of the sample (n=1058) was 36 years; 42% were male. The 6-month risk of discontinuation was significantly greater in patients with a low vs high initial dose (HR=1.357, 95% CI=1.070, 1.721; p=.012) and trended towards significance when comparing a medium vs high initial dose (HR=1.163, 95% CI=0.905, 1.494; p=.237). The largest difference in discontinuation rates between dose groups occurred after the first prescription.

Conclusions: Patients initiating ziprasidone therapy with an initial dose of at least 120 mg/day had better medication adherence compared with those initiating at lower doses. This may reflect improved efficacy at daily doses ≥120 mg.

Supported by a grant from Pfizer Inc.

References:
2. Stephane M, Barton S, Boutros NN: Auditory verbal hallucinatory pathways, and may suggest the involvement of the cortical cerebral glucose metabolism for auditory verbal hallucinations and the cerebellum and right orbitofrontal cortex. This feature does not support the hypothesis that auditory verbal hallucinations in acute schizophrenic patients reflect an abnormal activation of auditory-linguistic association cortices the content of the hallucinations they had experienced whilst in the first PET.

PET were acquired using an Advanced-Nxi Scanner (GEMS). Attenuations corrected images were standardized to the MNI PET template. Mean FDG uptake images of AH, R and AS were obtained. AH-R and AS-R difference images were calculated. Mean increased >5% were considered significant.

Results: The AH-R difference showed greater uptake during AH in anterior cingulate cortices, left orbitofrontal, left posterior frontal, posterior frontal parasagittal bilaterally, cerebellum, and some activation was also evident in left temporal cortex. The AS-R difference showed greater uptake during AS in right and left temporal cortex, left thalamus and some activation in left cerebellum and right orbitofrontal cortex.

Conclusions: Our findings showed a different pattern of regional cerebral glucose metabolism for auditory verbal hallucinations and for physiologic auditory activation. This feature does not support the hypothesis that auditory verbal hallucinations in acute schizophrenic patients reflect an abnormal activation of auditory-linguistic pathways, and may suggest the involvement of the cortical regions implicated in the generation of inner speech.

This study was supported by Janssen-Cilag.

References:

NR614  Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Auditory Hallucinations in First-Episode Schizophrenia: A FDG-PET Study Supported by Janssen-Cilag GMBH
Eduard Parellada, M.D., Department of Psychiatry, Hospital Clinic de Barcelona, Villarroel 170, Barcelona 08036, Spain; Mireia Font, Francisco Lomena, Ph.D., Deborah Pareto, Ph.D., Marc Simo, M.D., Emilio Fernandez-Egea, M.D., Miguel Bernado, M.D.

Educational Objectives:
- To test the hypothesis that endogenous auditory hallucinations involve activation of auditory/linguistic association cortices that are usually activated by externally presented speech.
- Methods: Eight neuroleptic-naive patients with first episode schizophrenia (DSM-IV criteria) with a prominent auditory hallucinations underwent three FDG-PET: a) while experiencing prominent and frequent auditory verbal hallucinations (AH); b) after clinical remission (R) taking a stable dose of antipsychotic medication (4-6 mg/day of risperidone); c) during bilateral acoustical stimulation (AS) through headphones with a spoken text that mimics the content of the hallucinations they had experienced whilst in the first PET.

-PET were acquired using an Advanced-Nxi Scanner (GEMS). Attenuations corrected images were standardized to the MNI PET template. Mean FDG uptake images of AH, R and AS were obtained. AH-R and AS-R difference images were calculated. Mean increased >5% were considered significant.

Results: The AH-R difference showed greater uptake during AH in anterior cingulate cortices, left orbitofrontal, left posterior frontal, posterior frontal parasagittal bilaterally, cerebellum, and some activation was also evident in left temporal cortex. The AS-R difference showed greater uptake during AS in right and left temporal cortex, left thalamus and some activation in left cerebellum and right orbitofrontal cortex.

Conclusions: Our findings showed a different pattern of regional cerebral glucose metabolism for auditory verbal hallucinations and for physiologic auditory activation. This feature does not support the hypothesis that auditory verbal hallucinations in acute schizophrenic patients reflect an abnormal activation of auditory-linguistic association cortices, and may suggest the involvement of the cortical regions implicated in the generation of inner speech.

This study was supported by Janssen-Cilag.

References:

NR616  Wednesday, May 5, 12:00 p.m.-2:00 p.m.
The Smoking Status and Clinical Characteristics in Patients With Chronic Schizophrenia
Bo-Hyun Yoon, M.D., NAJU National Hospital, Sanje Sampo, Namwon 520-830, Korea; Jin-Sang Yoon, M.D., Sung-Wan Kim, M.D., Myung-Kyu Kim, M.D., Ahn Bae

Educational Objectives:
- The Smoking Status and Clinical Characteristics in Patients With Chronic Schizophrenia
- At the conclusion of this session, the participant should recognize the smoking status and clinical characteristics of chronic schizophrenic patients.

Summary:
- Objective: Several studies have shown that schizophrenic patients have extremely high prevalence of smoking compared to those of other psychiatric disorders and general population. The reasons are unknown, but numerous factors may be interrelated. The authors aim was to evaluate the relationship between smoking status and clinical characteristics of the schizophrenic inpatients.

References:
Methods: Twenty-nine smokers and 45 non-smokers were assessed of their clinical status using the Positive and Negative Syndrome Scale (PANSS). Beck Depression Inventory (BDI). Hamilton Rating Scale for Depression (HAM-D), Simpson-Angus Rating Scale for Extrapyramidal Side Effects (SAS) and current Global Assessment of Functioning (CGAF). Other demographic and clinical data were also compared.

Results: There were no significant differences between smokers and non-smokers on the demographic and clinical histories. Smokers have more favorable scores on the total score of PANSS, HAM-D and CGAF. With correcting the effect the effect of marital status, duration of illness and dosages of antipsychotics, ANCOVA was done to analyze the effect of smoking and gender on the psychopathology. There were significant main effect of smoking on the total score of PANSS and the negative syndrome scale. Smokers also had more problems on alcohol-related histories before admission and more current consumptions of caffeine than non-smokers.

Conclusions: It was confirmed that smokers have more problems in the substance use of alcohol and caffeine, less severe psychopathology and more favorable levels of functioning. These results suggest that nicotine may improve the psychopathology of schizophrenia via activating mesolimbic dopamine pathway.

References:

NR617  Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Excess in Spring and Deficit in Autumn of Births in Italy of Males With Schizophrenia
Giuseppe Bersani, Psychiatry Department, Lasapienza University, Via di Torre Argentina 21, Rome, IT 00100, Italy; Daniela Pucci, Simona Gherardelli, Paolo Pancheri

Educational Objectives:
Objective is to increase knowledge about the potential role of seasonal factors in the increment of the risk of adulthood development of schizophrenia.

Summary:
The risk of schizophrenia is increased among individuals born in the late winter and early spring in the temperate latitudes of the Northern hemisphere. A number of plausible hypotheses advanced to explain such birth season effect suggest that an increased rate of pre- and perinatal brain injury caused by known seasonal variations in factors such as infectious diseases, nutritional deficiencies during pregnancy, perinatal exposure to alcohol, obstetric complications may contribute to the aetiology of schizophrenia. The aim of this study was to evaluate whether there were seasonal variations of births among psychotic patients in Italian population.

Birth dates of 1,270 inpatients with diagnosis of schizophrenia, other psychotic disorder and personality disorder/cluster A were studied using the chi square test.

A significant excess of births in spring (with a peak in May) and a deficit in autumn were found in the sample of male schizophrenics. No statistically significant results were found neither in the sample of female schizophrenics, nor in the sample with OPD and PD.

A possible explanation of this finding is that mostly Schizophrenia vulnerability genes interact with the considered environmental factors. Whatever is the factor responsible, it must act early enough in intrauterine development and also have a seasonal variation.

References:

NR618  Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Speed of Processing and Olfaction in Schizophrenia
Nora Goudsmit, M.A., Psychiatry Department, Columbia University, 1051 Riverside Drive, New York, NY 10032; Rachel Wolitzky, B.A., Cheryl M. Corcoran, M.D., Arielle Stanford, M.D., Eileen Alexander, B.S., Raymond Goetz, Ph.D., Dolores Malaspina, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize that among patients with schizophrenia there is an association between performance on Part A of the Trail Making Test and scores on the University of Pennsylvania Smell Identification Test beyond what is explained by age, sex, deficit syndrome, and general intellectual functioning.

Summary:
Background: Amid the various neurocognitive impairments documented in schizophrenia, smell identification deficits (SID) remain an undisputed and compelling finding. To determine how speed of processing is related to SID, we examined performance on the Trail Making Test.

Method: Our sample included 60 inpatients from the New York State Psychiatric Institute’s Schizophrenia Research Unit. We considered age, deficit syndrome, verbal IQ, and education in our analyses due to the documented relationship to smell identification ability. Smell identification was tested with the University of Pennsylvania Smell Identification Test (UPSIT), a forced-choice scratch-and-sniff odor identification task. The Trail Making Test primarily taps simple information processing and motor speed. Success on the test requires, sustained visual attention and effort, sequencing and aspects of working memory.

Results: UPSIT and Trails test mean scores respectively were 29.12 (SD = 4.60), Trails A seconds = 50.23 (SD = 29.09), Trails A errors = .17 (SD = .46), Trails B seconds = 140.92 (SD = 77.59), Trails B errors = 1.44 (SD = 2.82). Trails A errors and Trails A seconds accounted for a significant amount of the variance in UPSIT scores in regression analyses (R2 = .001, p = .008 and R2 = .051, p = .040).

Conclusion: Our novel finding that Trails A scores strongly and independently predict to UPSIT scores adds to the developing understanding of how neuropsychological performance and small identification ability are linked in schizophrenia. Connecting neurocognition to SID may prove to be an essential marker for schizophrenia research.

References:
**NR619 Wednesday, May 5, 12:00 p.m.-2:00 p.m.**

**Diabetes Schizophrenia Program: Structure and Initial Outcome Data**

Jean-Pierre Lindenmayer, M.D., *Manhattan Psychiatric Center, Wards Island, NY 10035*; Chandrika Tolia, M.D., Leon Balter, M.D., Alfred Blake, M.A., Anzalee Khan, M.S.

**Educational Objectives:**
After this presentation, participants will be able to better understand the effect of structured educational and monitoring strategies in the management of diabetes in patients with chronic schizophrenia.

**Summary:**

**Background:** Diabetes is increasing at an alarming rate in the US and in patients with schizophrenia, possibly association with the increased use of atypical antipsychotics. A specialized 25-bed inpatient diabetes schizophrenia program for the care of individuals with both schizophrenia and diabetes has been developed with the aim to create a supportive, educational and monitoring environment for both conditions and to prepare patients for independent illness management. We present the structure of the program and initial outcome data.

**Methods:** Treatment objectives are implemented through a structured 20-hour weekly group program, with focus on (1) education about diabetes and its treatment, (2) CBG fingerstick and glucometer reading skills using glucometers, (3) the calculation of NPH dosage, additional insulin and training for medication self-administration, (4) training in recording of all values, (5) implementation of dietary and exercise programs, and (6) monitoring of lipid values.

**Measures:** Data were collected on 22 inpatients who participated in the program over a six month period: (1) Psychiatric and diabetic medications and demographics; (2) Twice daily capillary blood glucose levels; (3) Daily insulin supplementation for high blood sugars; (4) HB1Ac; (5) Weights; (6) Ratings on a 15-item Diabetes Knowledge Scale.

**Results:** 22 (males = 18) inpatients with DSM IV diagnosis of schizophrenia and mean age of 50.77 years (range = 33 to 62) have been treated. There was a significant reduction in weight (F=5.31, p < .05), triglycerides (F=2.48 p < .05) and capillary blood glucose levels (F=2.24, p < .05). There were no significant changes in cholesterol and HB1Ac. A significant reduction in the Diabetes Knowledge Scale (F=11.317, p = .020, n = 6) was also seen.

**Conclusions:** Preliminary outcome data from an integrated diabetes/schizophrenia inpatient program showed significant improvements indicators of diabetes management. However, knowledge of diabetes decreased suggesting the need for development of enriched cognitive teaching on diabetes for this group of patients.

**References:**

**Goudsmit, M.A., Raymond Goetz, Ph.D., David J. Printz, M.D., Roberto Gil, M.D., Dolores Malaspina, M.D.**

**Educational Objectives:**
At the conclusion of this session, the participant should recognize that schizophrenia patients without family history of psychosis demonstrate better overall neurocognitive functioning than patients with a family history, specifically in the areas of speed of processing and perceptual-organizational skills.

**Summary:**

**Background:** Patients with schizophrenia have been found to differ in a number of domains based on family history status. Notably, previous research has indicated that patients with a family history of schizophrenia show a greater degree of cognitive and neuropsychological impairment than patients without a family history.

**Method:** We examined the neurocognitive performance, using the WAIS-R, of patients with a family history (familial) and without a family history (sporadic) to determine if differences exist that may help to explain the heterogeneous neuropsychological profile of the illness. 103 sporadic and 51 familial inpatients from the Schizophrenia Research Unit at the New York State Psychiatric Institute participated in the study.

**Results:** The family history groups did not differ with respect to gender, diagnosis, ethnicity, age, age of onset, education or duration of illness. Multivariate analyses, covarying for age of onset and education, showed the sporadic group performed significantly better than the familial group on the digit symbol (F = 4.241, df = 1, p = .041) and object assembly (F = 4.871, df = 1, p = .029) subtests, with a trend level difference in overall performance IQ score. (F = 3.46, df = 1, p = .065).

**Conclusions:** Overall, the sporadic group demonstrated better speed of processing, perceptual-organizational skills, and bottom down processing of visual stimuli. These group differences may help to explain the heterogeneous neuropsychological profile in the familial group in that these tasks involve visual attention and scanning, visuomotor control, and spatial processing and reasoning.

**References:**

**NR620 Wednesday, May 5, 12:00 p.m.-2:00 p.m.**

**Family History and WAIS-R Performance in Patients With Schizophrenia**

Rachel Wolitzky, B.A., Psychiatry Department, Columbia University, 1051 Riverside Drive, New York, NY 10032; Nora Goudsmit, M.A., Raymond Goetz, Ph.D., David J. Printz, M.D., Roberto Gil, M.D., Dolores Malaspina, M.D.

**Educational Objectives:**
At the conclusion of this session, the participant should understand the problem of medication adherence in schizophrenia and the role of insight in poor adherence.

**Summary:**

**Introduction:** Studies examining the relationship of insight to medication adherence have predominately utilized patient reports...
of adherence. There is little prospective data supporting the relationship of medication adherence and insight utilizing more objective assessments of adherence. We examined predictors of medication adherence in a cohort of 72 schizophrenia patients willing to take medication upon discharge from a state psychiatric hospital.

Methods: Subjects’ adherence was assessed at baseline and three months post hospital discharge using pill counts. Pill counts were conducted in the patients’ homes on unannounced visits. Adequate adherence was defined as taking 80% or more of the pills prescribed. We examined baseline insight, attitudes towards medication, therapeutic effectiveness of medication, complexity of treatment regimen, and cognitive functioning as predictors of medication adherence at three months.

Results: Results indicated that insight into having an illness and the benefits of taking medication were most strongly related to patients’ adherence during the immediate post discharge period.

Conclusion: Our data suggest that insight is not only related to medication refusal but rather to the amount of medication taken by the patient in the immediate post-discharge period. This suggests that insight is an important target for intervention with schizophrenia patients.

Funding Source(s): Unrestricted educational grant from AstraZeneca Pharmaceuticals

References:

NR622 Wednesday, May 5, 12:00 p.m.–2:00 p.m.
Aripiprazole and Perphenazine in Severe Treatment-Resistant Schizophrenia
Supported by Bristol-Meyers-Squibb and Otsuka Pharmaceutical Co., Ltd
Herbert Y. Meltzer, M.D., Department of Psychiatry, Vanderbilt University, 1601 23rd Avenue South, Suite 306, Nashville, TN 37212-8645; Mary J. Kujawa, M.D., William H. Carson, Jr., M.D., Joseph Stringfellow, M.S., Taro Iwamoto, Ph.D., Ronald N. Marcus, M.D., Elyse G. Stock, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to understand the efficacy and safety of aripiprazole compared with perphenazine in patients with treatment-resistant schizophrenia.

Summary:
Objective: To compare the efficacy of aripiprazole with that of perphenazine in treatment-resistant patients with pronounced symptoms of schizophrenia despite a trial of olanzapine or risperidone.

Methods: Patients with prospectively confirmed treatment-resistant schizophrenia (N=300) were randomized to six weeks of therapy with aripiprazole (15 or 30 mg/d) or perphenazine (8–64 mg/d). Treatment resistance was identified by patient history and confirmed by failure to respond to a 4–6 week trial of olanzapine or risperidone during an open-label treatment phase preceding randomization. Patients with most pronounced symptoms (upper tertile by PANSS-Total at randomization, N=90) were included in this analysis.

Results: For this group of extremely symptomatic patients (mean PANSS-Total, 123.7+/-18.5), the mean reduction in the PANSS-Total score at 6 weeks was 21.1+/-3.5 with aripiprazole and 13.5+/-3.8 with perphenazine, (P=NS). The response rate (prospectively defined as ≥30% decrease in PANSS-Total or CGI-I of 1 or 2) was 33% with aripiprazole and 29% with perphenazine.

Conclusion: In treatment-resistant schizophrenia patients who remained highly symptomatic after treatment with olanzapine or risperidone, therapy with aripiprazole or perphenazine nevertheless resulted in marked improvement of symptoms in about one third of the patients. The improvement seen during aripiprazole treatment was non-significantly greater than with perphenazine.

Funding Source(s): Bristol-Myers Squibb Company and Otsuka Pharmaceutical Co., Ltd

References:

NR623 Wednesday, May 5, 12:00 p.m.–2:00 p.m.
Fasting Glucose and Lipids in Patients With Schizophrenia Treated With Olanzapine Supported by Eli Lilly and Company
Thomas Hardy, M.D., Lilly Research, Eli Lilly Company, Lilly Corporate Center, DC5116, Indianapolis, IN 46285; Vicki P. Hoffmann, Pharm.D., Yong Lu, M.S., Suraia Y. Roychowdhury, Ph.D., Patrizia A. Cavazzoni, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize these findings are relevant to overall risk-benefit assessment, as is the finding of greater efficacy in controlling psychotic symptoms with olanzapine relative to ziprasidone treatment.

Summary:
Objectives: To characterize changes in fasting glucose and lipids in schizophrenia patients treated with olanzapine or ziprasidone. Methods: Patients were randomized to double-blind treatment with 10–20mg/day olanzapine (N=277) or 80–160mg/day ziprasidone (N=271) for 28 weeks. Mean baseline-to-endpoint changes in fasting plasma glucose, glucose and lipid values were compared within groups by t-test and between groups by sum of squares ANOVA. Temporal changes were analyzed by mixed model repeated measures. Correlations between metabolic and weight changes were done by Pearson correlation.

Results: Mean weight change at 28 weeks was +3.06kg for OLZ and -1.12kg for ZIP (p<0.001) although weight gain and loss occurred in both treatment groups. The percentages of patients with normal glucose at baseline (>126mg/dL) to abnormal at any time (>=126mg/dL) were not significantly different between groups (OLZ, 14.1% vs. ZIP, 15.9%; p=0.54). Using NCEP criteria, a significantly greater percentage of olanzapine-treated patients experienced treatment-emergent high triglycerides (16.9% vs. 2.6%; p<0.001). Changes in triglycerides but not glucose, were positively correlated with weight change in both groups.

Conclusion: Olanzapine treatment was associated with more patients in the ‘high’ triglycerides category; these changes were correlated with weight change. There were no between-group differences in clinically significant changes in glucose, LDL or HDL.

Funding Source(s): Supported by funding from Eli Lilly & Company

References:
1. Kane JM, Derg PH, Thakore J, et al: Olanzapine versus ziprasidone: results of the 28-week double-blind study in patients with...


NR624  Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Functional Status and Quality of Life in Latin-American Patients With Schizophrenia
Supported by Eli Lilly and Company
Sheila S.M. Assuncao, M.D., Neuroscience Department, Eli Lilly Brazil, Avenida Morumbi 8264, Brooklin 04703-002, Brazil; Andrew Hodge, M.S.C., Margret E. McBride, Ph.D., Alirio Perez Jo Presti, Daniel Toledo, M.D., Martin Dossenbach, M.D.

Educational Objectives:

The results of randomized controlled trials should be complemented by observational studies, like IC-SOHO, which evaluate the effectiveness of treatments in real clinical practice. Further, measurement of treatment outcomes in schizophrenia should not be limited to clinical symptoms but should include evaluation of psychosocial functioning and quality of life.

Summary:

Objective: To summarise changes in functional status and health related quality of life (HRQoL) in Latin American (LA) patients with schizophrenia after 12 months participation in a three-year global, observational study (FID-SN-HGJR).

Method: HRQoL (EuroQol EQ-5D, including VAS) and functional status (social, employment and residential) were determined for LA outpatients with schizophrenia. Data were adjusted for baseline differences and multivariate comparisons of olanzapine, risperidone and typical antipsychotic treatment were performed.

Results: Patients who remained on their originally prescribed monotherapy of olanzapine (n=803), risperidone (n=227) or typical antipsychotic treatment (n=183) for 12 months were compared. Following one year of therapy, patients in all treatment groups improved, but olanzapine was superior to typical antipsychotic treatment in terms of changes in total EuroQol score (p<0.001), health status (p<0.001), work status (p=0.0005) and social status (p=0.0002). Changes in total EuroQol (p=0.02) and health status (p=0.02) were also greater for olanzapine when compared to risperidone.

Conclusions: Our results confirm the positive influence of antipsychotic treatment on functional status and quality of life in patients with schizophrenia. Olanzapine was superior to typical antipsychotic therapy and showed greater improvement in HRQoL when compared with risperidone.

Funding Source(s): Supported by funding from Eli Lilly & Company

References:


NR625  Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Effect of Antipsychotic Change on Body-Mass Index or Weight in Minority Patients With Schizophrenia
Supported by Pfizer Inc.
Humberto Marin, M.D., Psychiatry Department, UMDNJ, Robert W. Johnson Medical School, 671 Hoes Lane, Room D-321, Piscataway, NJ 08855-1392; Matthew A. Menza, M.D., Anthony M. Tobia, M.D.

Educational Objectives:

At the conclusion of this session, the participant should recognize the increased risk of African- and Hispanic-American schizophrenics for overweight-obesity and consider treatment options that contribute the least to this risk.

Summary:

Introduction: One out of two American adults is now overweight or obese. Being a minority, especially African and Hispanic American, having schizophrenia, or using an antipsychotic seem to increase the risk. Ziprasidone, an atypical antipsychotic, has not been associated with weight gain in the general population or Caucasian patients.

Objective: Tests the effect of antipsychotic change to ziprasidone on metabolic parameters in African and Hispanic Americans.

Method: Open-label study in overweight (BMI≥25) Hispanic and African American outpatients with schizophrenia/psychotic disorder, switching from other antipsychotics to ziprasidone, with no additional dietetic or behavioral interventions. Main outcome measures are weight and BMI at six and 12 weeks. We have enrolled nine patients, eight of whom contributed data to this analysis, at six weeks. Of these, seven lost and one gained weight. Average weight at baseline was 227 lb, mean change at 6 weeks was –6.75 lb (SD=5.2), significant (paired student’s t-test –3.67, p<0.008). Average BMI at baseline was 34.25, mean change at 6 weeks was –1.125 (SD=0.64), significant (paired student’s t test –4.96, p<0.0016).

Conclusion: These data suggest that African and Hispanic-American overweight/obese patients with schizophrenia lose weight when switched to ziprasidone. If replicated in a controlled study, this finding would suggest that ziprasidone should be considered as an option in these patients.

Funding Source(s): Pfizer Inc

References:


NR626  Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Superiority of Olanzapine Versus Quetiapine in Improving Overall Functioning
Supported by Eli Lilly and Company
Sara Kollack-Walker, Ph.D., US Affiliate Medical Division, Eli Lilly And Company, Lilly Corporate Center, Indianapolis, IN 46285; Angela Hill, Ph.D., Hong Liu-Seifert, Ph.D., Bruce J. Kinon, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to discuss the effects of olanzapine and quetiapine on overall psychopathology and functioning during treatment of schizophrenia patients with prominent negative symptoms.
Objective: Schizophrenic outpatients with prominent negative symptoms are challenging patients in which to show functional improvement. This study compared olanzapine and quetiapine on overall psychopathology and functioning in these patients.

Methods: 346 patients with schizophrenia or schizoaffective disorder and prominent negative symptoms were randomized to six months, double-blind olanzapine (10–20 mg/day) or quetiapine (300–700mg/day). Overall psychopathology (Positive and Negative Syndrome Scale, Scale for Assessment of Negative Symptoms [SANS], and Clinical Global Impressions) and functioning (Global Assessment of Functioning and Quality of Life Scale) were compared with multivariate analysis of variance. Safety measures included laboratory analytes and extrapyramidal symptoms.

Results: Significantly more olanzapine-treated patients completed the study (52.6% OLZ vs 37.7% QUE, p<0.01); significantly more quetiapine-treated patients discontinued for lack of efficacy (OLZ 11.6% vs QUE 29.7%, p<0.001). Olanzapine-treated patients experienced significantly greater improvement in psychopathology (p=0.001) and overall functioning (p=0.04). Olanzapine-treated patients showed numerically, not statistically, greater improvement on SANS-total, the primary outcome measure (p=0.09). Both drugs were well-tolerated with no clinically-relevant differences in laboratory analytes or extrapyramidal symptoms.

Conclusions: Olanzapine-treated schizophrenia patients with negative symptoms experienced greater improvement in psychopathology and functioning over 6 months of therapy. No significant, clinically-relevant differences occurred in safety profiles of olanzapine and quetiapine.

Funding Source: Eli Lilly and Company

References:

NR627 Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Manual-Guided Use of Long-Acting Risperidone in Community-Based Settings
Supported by Janssen Pharmaceutica and Research Foundation
John P. Docherty, M.D., Department of Psychiatry, Comprehensive Neuroscience, 21 Bloomingdale Road, White Plains, NY 10605; Robert Jones, Ibrahim Turkoz, M.S., Lucy Mahalchick, Robert Lasser, M.D.

Educational Objectives:
At the conclusion of this presentation, participants should be able to recognize the effectiveness of manual use for optimizing community-based care with long-acting risperidone, as well as the clinical benefits and patient satisfaction with long-acting risperidone treatment in this setting.

Summary:
Objective: This study employed a manual to optimize community-based care with long-acting risperidone (LAR). A novel research treatment-manual assessment methodology evaluated its effectiveness.

Method: A 12-week, open-label, multicenter study in CMHCs enrolled 60 stable outpatients with schizophrenia or schizoaffective disorder switched from oral risperidone to LAR. The primary objective was to assess the usefulness of, and adherence to, the LAR manual. Patient experience also was assessed, using CGI, SQLS and measures of safety, tolerability and patient satisfaction.

Results: Most (90%) of CMHC staff rated the treatment manual “quite a bit” or “extremely” informative. Adherence by clinicians (89% to 100%) and patients (87% fully-adherent) was excellent. Significant improvement on the CGI-S was observed as early as week 8 (P<0.05), and LAR was well tolerated. Patients were satisfied with LAR treatment (86% versus 63% with oral antipsychotics); 70% found LAR “better” or “much better” than oral risperidone. Concern about pain decreased significantly over the study (P=0.041). Convenience and ease were the most frequently cited reasons favoring LAR.

Conclusions: CMHC staff considered the treatment manual valuable, and both patients and staff adhered to manual guidelines. Additionally, LAR was well tolerated, usually preferred to oral atypicals, and associated with significant clinical improvement, even in previously stable patients.

Funding Source(s): Supported by Janssen Pharmaceutica Products.

References:
References:


NR629 Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Clinical Improvement With Long-Acting Risperidone: No Impact of Race
Supported by Janssen Pharmaceutica and Research Foundation

Ronald Urioste, M.S., Janssen Pharmaceutica, 1125 Trenton-Harbourton Road, Titusville, NJ 08560; Cynthia Bossie, Ph.D., Young Zhu, Ph.D., Natalie Ciliberto, Pharm.D., Bo Trinh, Pharm.D., Robert Lasser, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to describe the impact of race on clinical improvement with long-acting risperidone treatment.

Summary:
Objective: This analysis assessed the effect of race on response to long-acting injectable risperidone treatment in patients with schizophrenia or schizoaffective disorder.
Method: In a 12-week, randomized, double-blind study, patients with schizophrenia or schizoaffective disorder received placebo or long-acting risperidone (25, 50, or 75 mg every two weeks). Demographic data identified patients as Caucasian, African American, or ‘other.’ Because psychotic symptoms were assessed by the Positive and Negative Syndrome Scale (PANSS); movement disorders by the Extrapyramidal Symptom Rating Scale (ESRS); adverse events (AEs) were reported spontaneously.
Results: Data were available for 193 Caucasian (44%), 174 (40%) African-American, and 72 (16%) ‘other’ (Hispanic, Asian, other) patients. Baseline characteristics were similar between racial groups, as were study completion rates (overall, 30% placebo, and 46% long-acting risperidone). There was a significant effect of treatment (P<0.001), but not race, on improvement in PANSS total scores from baseline to endpoint. ESRS scores were low throughout the study, with no significant effects of race observed. Overall rates of AEs were similar between racial groups, but discontinuations due to AEs with long-acting risperidone treatment were lower for African-American (14.5%) than for Caucasian (28.6%) or “other” (33.3%) patients.
Conclusions: Race did not appear to impact the efficacy and tolerability of long-acting risperidone.

Supported by Janssen Pharmaceutica Products, L.P.

References:


NR630 Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Duration of Exposure to Olanzapine and Risperidone and Development of DKA
Supported by Janssen Pharmaceutica and Research Foundation

Krishnan Ramaswamy, Ph.D., Janssen Pharmaceutica, 1125 Trenton-Harbourton Road, Titusville, NJ 08560; Chris Kozma, Ph.D., Henry A. Nasrallah, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize some of the differential risk factors for developing DKA including duration of exposure to antipsychotic therapy.

Summary:
Objective: Assess relationship of duration of exposure to antipsychotics and development of DKA in patients receiving risperidone or olanzapine.
Methods: Retrospective cohorts of olanzapine (51,267) and risperidone (51,285) patients dispensed no other atypical antipsychotic for at least six months were evaluated for DKA diagnoses using 1997–2000 California Medicaid data. DKA cases diagnosed after starting the atypical antipsychotic were defined “potentially attributable” if an antipsychotic was dispensed within 45 days prior to diagnosis. A logistic regression model predicting DKA was evaluated using indicators for antipsychotic, drug exposure, age, race, mental health diagnoses and prior diagnosis of diabetes.
Results: The incidence rates of DKA were 31 for the risperidone group and 55 for the olanzapine group. In the logistic regression model, odds of DKA were 1.6 times greater in the olanzapine group and increased with exposure. For drug exposure greater than 30, 90 and 180 days, odds of DKA were 1.7, 2.4 and 3.5 times greater for olanzapine than risperidone, respectively. Prior diagnosis of diabetes consistently predicted DKA (approximately 9 times greater risk). African-American ethnicity and diagnosis of schizophrenia were significant in some models.
Conclusions: The odds of developing DKA increased with exposure to olanzapine relative to risperidone after adjusting for covariables.
Funding Source(s): Janssen Pharmaceutica Products, LP

References:


NR631 Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Long-Acting Risperidone: Redefining Symptomatic Remission in Schizophrenia
Supported by Janssen Pharmaceutica and Research Foundation

John M. Kane, M.D., Department of Psychiatry, Hillside Hospital, 75-59 263rd Street, Glen Oaks, NY 11004-1150; Robert Lasser, M.D., Cynthia Bossie, Ph.D., Young Zhu, Ph.D., Lucy Mahalchick, Georges Gharabawi, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize some of the differential risk factors for developing DKA including duration of exposure to antipsychotic therapy.

Summary:
Objective: Assess relationship of duration of exposure to antipsychotics and development of DKA in patients receiving risperidone or olanzapine.
Methods: Retrospective cohorts of olanzapine (51,267) and risperidone (51,285) patients dispensed no other atypical antipsychotic for at least six months were evaluated for DKA diagnoses using 1997–2000 California Medicaid data. DKA cases diagnosed after starting the atypical antipsychotic were defined “potentially attributable” if an antipsychotic was dispensed within 45 days prior to diagnosis. A logistic regression model predicting DKA was evaluated using indicators for antipsychotic, drug exposure, age, race, mental health diagnoses and prior diagnosis of diabetes.
Results: The incidence rates of DKA were 31 for the risperidone group and 55 for the olanzapine group. In the logistic regression model, odds of DKA were 1.6 times greater in the olanzapine group and increased with exposure. For drug exposure greater than 30, 90 and 180 days, odds of DKA were 1.7, 2.4 and 3.5 times greater for olanzapine than risperidone, respectively. Prior diagnosis of diabetes consistently predicted DKA (approximately 9 times greater risk). African-American ethnicity and diagnosis of schizophrenia were significant in some models.
Conclusions: The odds of developing DKA increased with exposure to olanzapine relative to risperidone after adjusting for covariables.
Funding Source(s): Janssen Pharmaceutica Products, LP

References:

Summary:

Objective: Essential features of schizophrenia are defined as the presence and persistence of characteristic symptomatology. Symptomatic remission, however, is poorly defined. The objective of this analysis was to apply expert-proposed symptom remission criteria to data from a long-acting risperidone study.

Methods: Data were from an open-label, 50-week study of long-acting risperidone in 578 stable patients with schizophrenia or schizoaffective disorder. Remission was defined as a score of = 3 (mild or less) concurrently on each of these items on the Positive and Negative Syndrome Scale: delusions (P1), conceptual disorganization (P2), hallucinatory behavior (P3), unusual thought content (G9), mannerisms and posturing (G5), blunted affect (N1), passive/apathetic social withdrawal (N4), and lack of spontaneity and conversation flow (N6).

Results: Of 578 stable patients, 394 (68%) did not meet symptomatic remission criteria at study entry. After treatment, 82 (21%) of these patients met symptomatic remission criteria for =6 months with significant improvements in quality-of-life measures. Of 184 patients who met symptomatic remission criteria at baseline, 156 (85%) maintained it at endpoint, with significant efficacy benefits.

Conclusions: Many patients considered stable at baseline achieved a predefined level of symptomatic remission after treatment with long-acting risperidone, suggesting further validation of these criteria is warranted.

Funding Source(s): Supported by Janssen Pharmaceutical Products, L.P.

References:


NR632 Wednesday, May 5, 12:00 p.m.-2:00 p.m.

Dopamine Receptor Analysis in Leukocytes in Schizophrenia

Marco A. Romano-Silva, Ph.D., Pharmacology Department, Federal University, Antonio Carlos 6627-UFMG-ICB, Belo Horizonte, MG 31270-901, Brazil; Kleber Pinto, M.S.C., Malderez Dutra, Ph.D., Humberto Corrêa, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should recognize the possibility of studying peripheral markers in schizophrenia.

Summary:

Objective: The dopaminergic hypothesis of schizophrenia has been strongly supported by the fact that most of the antipsychotic drugs block dopamine receptors. To assess the changes in dopamine receptors, an easily accessible peripheral marker is needed, and the dopamine receptor of peripheral leukocytes may be a possible candidate.

Methods: We tested D3 and D4 dopamine receptor antibody staining through flow cytometry in 45 hospitalized schizophrenic patients, and compared with 45 controls.

Results: We found no differences between schizophrenic patients and healthy controls in D3 or D4 dopamine receptors staining in any type of leukocyte tested. However, we observed differences between patients with higher versus minor symptomatology in BPRS in both D3 (p=0.000) and D4 (p=0.035) staining. These alterations were mainly due to delirious and paranoid subscales of BPRS. D3 and D4 staining were also negatively correlated with disorganized BPRS sub scale (p=0.000).

Conclusion: Our results arise the perspective that a peripheral measurable marker would help in research, but also in clinical conduction of schizophrenia.

References:


NR633 Wednesday, May 5, 12:00 p.m.-2:00 p.m.

Self-Reported Body Weight Status and Dieting Practices in Schizophrenia Outpatients

Martin Strassnig, M.D., Psychiatry Department, University of Pittsburgh, 3811 O’Hara Street, Pittsburgh, PA 15213; Jaspreat S. Brar, M.D., Rohan Ganguli, M.D.

Educational Objectives:

At the conclusion of this session, the participant should recognize the relationship of actual body weight, self-perception of body weight, and weight loss attempts in schizophrenia patients.

Summary:

Introduction: Serious health risks are associated with overweight, yet effective weight loss measures are scarce. To better address this problem, we examined the relationship between body weight perception, desire to lose weight; dieting; and actual weight and height in schizophrenia patients.

Methods: Information on self-reported weight perception, desire to lose weight and weight loss attempts of n=147 patients was obtained using methods as employed in NHANES III. Body weight and height were measured, BMI was calculated.

Results: Perception of body weight and desire to lose weight were correlated to BMI. Both obese female and male subjects (BMI > 30) were aware of their weight status. Whereas overweight females (BMI 25–29.9) accurately perceived themselves as such, corresponding males did not, and neither wanted nor tried to lose weight. Dieting was the most popular measure (n=67; 80% of sample). Only a third of subjects (n=27; 34.4%) used a combination of diet and exercise. Among women, questionable weight loss practices were common.

Conclusions: Obese patients (BMI ≥30) were aware of their weight status and wanted to lose weight. Measures employed to lose weight appeared not always appropriate and safe. There is a need for easy-to-administer yet formal weight loss programs.

References:


NR634 Wednesday, May 5, 12:00 p.m.-2:00 p.m.

Adjunctive Divalproex Sodium Lowers Cholesterol Elevation With Olanzapine Supported by Abbott Laboratories

Mahtab Jafari, Pharm.D., Neuroscience Department, Abbott Laboratories, 33 Bargemon, Newport Coast, CA 92657; Ping Jiang, M.S., Daniel E. Casey, M.D.
Educational Objectives:

At the conclusion of this session, the participant should be able to examine the effect of olanzapine, risperidone, divalproex plus olanzapine, and divalproex plus risperidone on total cholesterol.

Summary:

Introduction: The metabolic complications of atypical antipsychotics, especially their effects on weight, serum lipids and glucose, are major concerns for clinicians. Divalproex has achieved wide use as an adjunctive therapy for schizophrenia. Preliminary data suggest that this agent may not have a significant impact on serum lipids or glucose.

Methods: A retrospective analysis of a double blind, randomized, and multicenter study that assessed the efficacy and safety of divalproex when combined with risperidone and olanzapine was conducted. Two hundred forty nine patients were randomized to receive olanzapine monotherapy (n=65), divalproex plus olanzapine (n=66), risperidone monotherapy (n=60), or divalproex plus risperidone (n=58).

Results: There were no statistically significant baseline differences between the treatment groups in regards to demographic data. The changes in total cholesterol in four groups were: +26.62 mg/dL for olanzapine, +0.87 mg/dL for divalproex plus olanzapine, +9.64 mg/dL for risperidone, and +13.44 mg/dL for divalproex plus risperidone. Patients in the olanzapine group had the highest rate of shift from a normal total cholesterol (<200 mg/dL) to a high total cholesterol (≥200 mg/dL). The addition of divalproex resulted in less increase in total cholesterol. There were no significant changes in glucose in any group.

Conclusion: Adding divalproex to olanzapine or risperidone resulted in a decrease or no change in total cholesterol. Cholesterol lowering effects of DVPX has also been reported in recent preliminary reports in patients with bipolar disorder, and are reconfirmed in this study.

Supported by Abbott Laboratories.

References:

NR635  Wednesday, May 5, 12:00 p.m.-2:00 p.m.

Long-Term Long-Acting Risperidone: QoL and Functioning in Schizophrenia

Supported by Janssen Pharmaceutica and Research Foundation

Stephen Rodriguez, M.S., Janssen Pharmaceutica, 1125 Tranton-Harbourton Road, Titusville, NJ 08560; Robert Lasser, M.D., Ibrahim Turkoz, M.S., Ronald Urioste, M.S., Emilie J. Burks, Pharm.D., Georges Gharabawi, M.D.

Educational Objectives:

At the conclusion of this presentation, participants should be able to describe interim data on quality of life and functioning during maintenance treatment with long-acting risperidone in patients with schizophrenia or schizoaffective disorder.

Summary:

Objective: Improvements in quality of life (QoL) and patient functioning are important goals of long-term treatment of psychotic illness. The objective of this analysis was to examine the impact of maintenance therapy with long-acting risperidone on QoL and functioning in patients with schizophrenia or schizoaffective disorder.

Method: Data are from an ongoing 52-week, prospective, randomized, double-blind, multicenter study in 176 previously stable patients with schizophrenia or schizoaffective disorder randomized to long-acting risperidone 25 or 50 mg/2 weeks. Quality of life and functionality were assessed using the Schizophrenia Quality of Life Scale (SQLS), the Strauss-Carpenter Level of Functioning Scale (LOF), and the Personal and Social Performance Scale (PSP).

Results: The study includes 176 patients (60% male, mean age, 41.7±10.6 years). At baseline, the mean (SD) scores for items on the SQLS were psychosocial subscale, 42.1±20.3; energy/motivation subscale, 42.3±17.3 and symptom/side-effect subscale, 34.7±15.5. The mean LOF total score was 21.1±5.8 and the mean LOF 4-item score was 10.1±2.4. The baseline PSP score was 61.9±14.3. Interim data are presented here.

Conclusions: Previous studies with long-acting risperidone have preliminarily indicated improvements in QoL. This randomized, double-blind 52-week study provides an in-depth investigation of QoL and functionality.

Supported by Janssen Pharmaceutica Products, L.P.

References:

NR636  Wednesday, May 5, 12:00 p.m.-2:00 p.m.

Association Between Viral Infections and First Episode of Schizophrenia

Guido Mazzotti, M.D., Mental Health Department, UPCH-U Johns Hopkins, 624 N. Broadway, Suite 894, Baltimore, MD 21205; Carla Gallo, M.S.C., Silvana Sarabia, M.D., Giovanni Poletti, Abel Sagastegui, M.D., E. Fuller Torrey, M.D., Robert H. Yolken, M.D.

Educational Objectives:

At the conclusion of this session, the participant should recognize the association between the first episode of schizophrenia and viral infection seropositivity focusing on Herpes virus, and to discuss other associations and adjustments as well as the implications of these findings for psychosis’ causality.

Summary:

Background: Schizophrenia has been associated to early infections (intrauterine), latent infections, and re-infections of viruses. Recent findings have focused the attention on Herpes viruses and Toxoplasmosis.

Objectives: To determine the association between seropositivity to Herpes Simplex Virus type 2 (HSV-2), Cytomegalovirus (CMV), and other viruses with first episode of schizophrenia (FES).

Methods: Individually matched case-control study, DSM-IV criteria for diagnosis, N=122. Procedures were done at the Clinical Network of Universidad Peruana Cayetano Heredia (clinical sites, laboratories), Lima, Peru. Sex, age, SES, season and place of birth, and current place of residence matched cases and controls. After basic exploration of data we used conditional logistic regression for analysis of association.

Results: FES was significantly associated with HSV-2 seropositivity (OR: 4.8; p = 0.001; 95% CI: 1.9, 11.6), and with CMV Seropositivity (OR: 5.7; p = 0.006; 95% CI: 1.7, 13.6). Additional
adjustments by family antecedents of mental disorders, and two indicators of sexual risk behavior did not have significant influence on the associations. Herpes Simplex Virus type 1 was marginally associated with FES. Epstein Barr virus and Varicella zoster virus were not associated with FES.

**Conclusion:** First-episode of schizophrenia is significantly associated with serological evidence of infections with HSV-2 and Cytomegalovirus.

**Funding Source(s):** Stanley Medical Research Institute

**References:**


**NR637** Wednesday, May 5, 12:00 p.m.-2:00 p.m.

**Safety Profile of Aripiprazole in Psychosis of Alzheimer's Dementia: Pooled Data**

**Supported by Bristol-Myers-Squibb and Otsuka Pharmaceutical Co., Ltd.**

Elyse G. Stock, M.D., Neurosciences Department, Bristol-Myers Squibb Company, 5 Research Parkway, Wallingford, CT 06492-7660; Christopher Breder, M.D., Harry Goyaerits, M.S.C., William H. Carson, Jr., M.D., Taro Iwamoto, Ph.D., Dariene Jody, M.D., Richard Wilber, M.D.

**Educational Objectives:**

At the conclusion of this presentation, the participant should be able to understand the safety and tolerability profile of aripiprazole in elderly patients with psychosis of Alzheimer's dementia.

**Summary:**

**Objective:** To characterize the safety and tolerability of aripiprazole in elderly patients.

**Methods:** Safety data from two 10-week double-blind placebo-controlled trials in patients with psychosis of AD were pooled (N=458). The dosing regimen of aripiprazole consisted of titration in the 2-15 mg/d range.

**Results:** Discontinuation rates due to adverse events were 8% with placebo and 12% with aripiprazole. There was no clear pattern of adverse events leading to discontinuation in either group. The most common adverse event reported in both groups was accidental injury: 18% with placebo and 15% with aripiprazole. The only adverse event that occurred in the aripiprazole group at a frequency greater by at least 5% than in the placebo group was somnolence (3% placebo vs 11% aripiprazole). Most cases of somnolence reported with aripiprazole were mild to moderate and only two patients discontinued therapy because of this adverse event. EPS-related adverse events were reported in 4% of patients treated with placebo and 5% of those treated with aripiprazole.

**Conclusions:** Data from two trials in patients with psychosis of AD indicate that aripiprazole is safe and well tolerated in this patient population, with low rates of EPS and discontinuation due to adverse events.

**Funding Source(s):** Bristol-Myers Squibb Company and Otsuka Pharmaceutical Co., Ltd.

**References:**


**NR638** Wednesday, May 5, 12:00 p.m.-2:00 p.m.

**Cortical-Striatal-Thalamic and Startle-Blink Abnormalities in Schizotypals**

Erin A. Hazlett, Ph.D., Department of Psychiatry, Mt. Sinai Medical School, One Gustave Levy Place, Box 1505, New York, NY 10029; Monte S. Buchsbaum, M.D., Bradley Buchsbaum, Ph.D., Michelle Romero, M.A., Antonia S. New, M.D., Cheuk Y. Tank, Ph.D., Larry J. Siever, M.D.

**Educational Objectives:**

At the conclusion of this session, the participant should be able to demonstrate an understanding of: (1) psychophysiological measurement of sensorimotor gating and its modulation by attentional processing as indexed by prepulse inhibition (PPI) of the startle eyeblink response; and (2) current PPI and functional brain imaging (fMRI, PET) findings in schizotypy.

**Summary:**

Several studies indicate that prepulse inhibition (PPI) of startle is modulated by attention and individuals within the schizophrenia spectrum exhibit PPI deficits. Animal models of PPI indicate the role of cortical- striatal-thalamic circuitry in PPI modulation. In this study, unmedicated schizotypal personality disorder (SPD) patients (n=15) and matched controls received event-related fMRI (GE Siemens Allega head-dedicated 3T scanner) and psychophysiological measurement of PPI. The task involved an attention-to-prepulse paradigm with a series of attended and ignored tones that served as prepauses to the acoustic startle stimulus. Subjects were instructed to silently count the number of longer-than-usual tones of a specified pitch. The startle stimulus was presented during some prepauses of each type and between some prepauses to measure baseline startle. Healthy controls showed greater PPI during the attended than the ignored prepauses, replicating attentional modulation of PPI. In contrast, SPD patients failed to show this pattern. The control group also had significantly greater difference scores (attend minus ignore condition) for BOLD response in anterior cingulate, caudate, and anterior nucleus region of the thalamus compared with the SPD group. These findings suggest that schizophrenia-spectrum abnormalities in cortical-striatal-thalamic circuitry underlie deficient attentional modulation of PPI.

**References:**


**NR639** Wednesday, May 5, 12:00 p.m.-2:00 p.m.

**Drug Consumption in Hospitalized Patients With Schizophrenia**

Edorta Elizagarate, Ph.D., UPR, H. Psiquiatrico Alava, Alava 43, Vitoria 01006, Spain; Pedro Sanchez Gomez, M.D., Natalia Ojeda del Pozo, Ph.D., Ana B. Yoller Elburgo, M.D., Esther Ibarrola, M.D., Jesus Ezcurra Sanchez, Ph.D.

**Educational Objectives:**

After presentation, all readers will be able to understand the relation between differential use of drugs by chronic hospitalized patients with schizophrenia, course of illness and presence of psychiatric, cognitive, and functional symptoms.
Introduction: Drug abuse is a key aspect in the differentiation and treatment of patients with schizophrenia (Dixon, 1991). However, it remains unclear the relation among drug abuse, psychiatric symptoms and chronicity.

Hypothesis: Drug abuse in chronic schizophrenia is related to evolution, negative symptoms, low cognitive resources and functional outcome.

Methods: 98 patients with Schizophrenia were examined, including clinical interview, blood analysis, and 7 clinical scales (PANSS, DAS-WHO, GAF-EAG, Insight-David, Social Premorbid Adjustment (Cannon-Spoor), CGI). Drug consum was stabilized by blood analysis and Likert Scale Substance Abuse (alcohol, cannabis, cocaine, methadone, amphetamines, opiates) administered to patients and close relatives for estimation of consum one year before the onset of illness, and consum during last four months.

Results & Conclusions: Drug consum in our sample is very high, specially for alcohol and cannabis, though multiple-consum is more frequent, opiaces/methadone seems to interact differently with symptoms than other drugs. The abuse is independent of education level, premorbid adjustment (crr=-0.2656; p=0.528), and insight (crr=0.0147; p=0.867). Abuse is higher in younger patients (crr=-0.4929; p=0.000), less severe psychiatric symptoms (by CGI (crr=-0.4024; p=0.000), and time (crr=-0.4418; p=0.000)/number of hospitalization (crr=-0.2293; p=0.026). Consum is associated with negative symptoms (crr=-0.3400; p=0.001), and executive functioning (crr=-0.4650; p=0.002). The self-medication hypothesis is not confirmed with our results, which lead to the need for a reformulation of the vulnerability hypothesis. 2 (statistics included refer to cannabis as example)

Patients are 36,95 mean age (SD + 11,06) men (86% of sample) with a mean time of hospitalization was 676,95 days (SD + 452,77), and mean number of hospitalizations was. Mean age of onset of illness for the sample was 21,74 (SD + 5.91) and 15,29 (SD+9,57) of evolution.

References:

Educational Objectives:
At the conclusion of this session, the participant should be able to describe the efficacy and safety of long-acting risperidone in young adult patients with schizophrenia.

Summary:

NR640 Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Ziprasidone, Risperidone, and Haloperidol Differences: 1231-IBZM SPECT Study Supported by Pfizer Inc.
Iluminada Corrió, Ph.D., Psychiatry Department, Sant Pau Hospital, St. Antoni Claret 167, Barcelona 08025, Spain; Dolores Puigdemont, Ph.D., Juan C. Pascual, Ph.D., Marc Ferrer, Ph.D., Victor Perez, Ph.D., Ana Catalfau, Ph.D., Enrique Alvarez, M.D.

Educational Objectives:
The atypical antipsychotic profile have been related to an effective low D2 receptor occupancy with a benefit for the improvement of extrapyramidal side effects and negative symptoms. Our results support differences between typical and atypical antipsychotic in D2 receptor blockade.

Summary:
Objective: The aim was to investigate D2 receptor occupancy differences among ziprasidone, risperidone and haloperidol, and the relationship of D2 receptor occupancy to clinical efficacy and EPS, with 123I-IBZM SPECT.

Methods: 38 patients with a DSM-IV diagnosis of schizophrenia were recruited for the study. There were three groups depending on the antipsychotic treatment received: haloperidol (n=10), ziprasidone (n=10), and risperidone (n=18). Clinical efficacy was assessed by means of PANSS and BPRS. EPS was evaluated by the Simpson-Angus scale scores.

Results: (1) D2 receptor occupancy differed significantly among the treatment groups: haloperidol 73.5±8.8%, risperidone 62.7±13.9%, and ziprasidone 51.3±11.5%. Post-hoc analysis revealed differences only between the ziprasidone and haloperidol group. (2) The scores obtained on the Simpson-Angus scale were significantly different only when comparing the haloperidol and ziprasidone group. (3) A minimal threshold above 60% of D2 receptor occupancy was achieved in responders in the haloperidol and risperidone group, however this was below 60% in the ziprasidone group.

Conclusions: (1) Ziprasidone was clearly better than haloperidol in the EPS profile, and risperidone was in a range between both of them. (2) An atypical profile was demonstrated only in the ziprasidone group that showed an effective blockade below 60%.

References:

NR641 Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Long-Acting Risperidone in Young Adults With Schizophrenia or Schizoaffective Disorder Supported by Janssen Pharmaceutica and Research Foundation
Robert Lasser, M.D., CNS Medical Affairs, Janssen Pharmaceutica, 1125 Trenton-Harbourton Road, Titusville, NJ 08560-0200; Cynthia Bossie, Ph.D., Young Zhu, Ph.D., Natalie Ciliberto, Pharm.D., Jacquelyn McLemore, M.D., John M. Kane, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to describe the efficacy and safety of long-acting risperidone in young adult patients with schizophrenia.

Summary:

NR640 Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Ziprasidone, Risperidone, and Haloperidol Differences: 1231-IBZM SPECT Study Supported by Pfizer Inc.
Iluminada Corrió, Ph.D., Psychiatry Department, Sant Pau Hospital, St. Antoni Claret 167, Barcelona 08025, Spain; Dolores Puigdemont, Ph.D., Juan C. Pascual, Ph.D., Marc Ferrer, Ph.D., Victor Perez, Ph.D., Ana Catalfau, Ph.D., Enrique Alvarez, M.D.

Educational Objectives:
The atypical antipsychotic profile have been related to an effective low D2 receptor occupancy with a benefit for the improvement of extrapyramidal side effects and negative symptoms. Our results support differences between typical and atypical antipsychotic in D2 receptor blockade.

Summary:
Objective: The aim was to investigate D2 receptor occupancy differences among ziprasidone, risperidone and haloperidol, and the relationship of D2 receptor occupancy to clinical efficacy and EPS, with 123I-IBZM SPECT.

Methods: 38 patients with a DSM-IV diagnosis of schizophrenia were recruited for the study. There were three groups depending on the antipsychotic treatment received: haloperidol (n=10), ziprasidone (n=10), and risperidone (n=18). Clinical efficacy was assessed by means of PANSS and BPRS. EPS was evaluated by the Simpson-Angus scale scores.

Results: (1) D2 receptor occupancy differed significantly among the treatment groups: haloperidol 73.5±8.8%, risperidone 62.7±13.9%, and ziprasidone 51.3±11.5%. Post-hoc analysis revealed differences only between the ziprasidone and haloperidol group. (2) The scores obtained on the Simpson-Angus scale were significantly different only when comparing the haloperidol and ziprasidone group. (3) A minimal threshold above 60% of D2 receptor occupancy was achieved in responders in the haloperidol and risperidone group, however this was below 60% in the ziprasidone group.

Conclusions: (1) Ziprasidone was clearly better than haloperidol in the EPS profile, and risperidone was in a range between both of them. (2) An atypical profile was demonstrated only in the ziprasidone group that showed an effective blockade below 60%.

References:
study (baseline 66.98±20.58, endpoint 57.19±18.60; P<0.001). PANSS positive, negative, disorganized thoughts, uncontrolled hostility/excitement, and anxiety/depression scores improved significantly at endpoint. Extrapyramidal Symptom Rating Scale patient ratings and physician-rated parkinsonism scores decreased significantly at endpoint (P<0.001). Mean Visual Analog Scale pain scores were low throughout the study, and decreased further at endpoint (P<0.001). Most common adverse events were insomnia (27.3%), psychosis (21.8%), anxiety (20.9%), hyperkinesia (20.0%), depression (17.3%), and headache (15.5%).

Conclusion: These data suggest that long-acting risperidone can provide further symptom improvement in stable patients with early psychotic illness.

Funding Source(s): Supported by Janssen Pharmaceutica Products, L.P.

References:

NR642 Wednesday, May 5, 12:00 p.m.–2:00 p.m.
Long-Acting Risperidone in Stable Patients With Schizophrenia Switched From Oral Treatment With Quetiapine
Supported by Johnson & Johnson and Janssen Pharmaceutica and Research Foundation

Robert Lasser, M.D., CNS Medical Affairs, Janssen Pharmaceutica, 1125 Trenton-Harbourton Road, Titusville, NJ 08560-0200; Ann Clark, Ed Crumbley, B.A., Young Zhu, Ph.D., Sally A. Barry, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to demonstrate a significant difference of bone density between schizophrenic patients and normal controls.

Most schizophrenic patients take antipsychotics for a long time, and they have a higher serum prolactin level compared with the general population. It was postulated that osteoporosis or a lower bone density might be followed by a long-term prolactinemia. We collected data on 177 schizophrenic patients in Taiwan (best estimate diagnosis by DSM-IV criteria), who have at least more than two years of antipsychotics history. We also recruited 647 sex-matched normal controls who had no exposure history to antipsychotics in Taiwan. The bone density was evaluated by a sonogram detector (QUS-II) and recorded in the unit of BUS. After stratified by ages, the mean bone density of schizophrenic patients is statistically higher than normal controls in age 30–39 and age 40–49 groups separately (93.2 vs 85.2 with p-value <0.01, and 91.2 vs 84.1 with p-value < 0.001). This result was out of our previous expectation, and more samples or similar studies are required to confirm this finding. It is suggested there is an unknown protective effect of bone density loss for schizophrenic patients aged 30–49 in Taiwan.

References:

NR643 Wednesday, May 5, 12:00 p.m.–2:00 p.m.
The Comparison of Bone Density Between Patients With Schizophrenia and Controls
Tsuo-Hung Lan, M.D., Psychiatry Department, TYPC, 71 Long-Show Street, Tao-Yuan 330, Taiwan; Hsieh-Jane Chiu, M.D., Nan-Ping Yang, M.D., Jin-Han Sou, M.D., Jenn-Huei Renn, M.D., Pesus Chou, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to demonstrate a significant difference of bone density between schizophrenic patients and normal controls.

Most schizophrenic patients take antipsychotics for a long time, and they have a higher serum prolactin level compared with the general population. It was postulated that osteoporosis or a lower bone density might be followed by a long-term prolactinemia. We collected data on 177 schizophrenic patients in Taiwan (best estimate diagnosis by DSM-IV criteria), who have at least more than two years of antipsychotics history. We also recruited 647 sex-matched normal controls who had no exposure history to antipsychotics in Taiwan. The bone density was evaluated by a sonogram detector (QUS-II) and recorded in the unit of BUS. After stratified by ages, the mean bone density of schizophrenic patients is statistically higher than normal controls in age 30–39 and age 40–49 groups separately (93.2 vs 85.2 with p-value <0.01, and 91.2 vs 84.1 with p-value < 0.001). This result was out of our previous expectation, and more samples or similar studies are required to confirm this finding. It is suggested there is an unknown protective effect of bone density loss for schizophrenic patients aged 30–49 in Taiwan.

References:
Objective: While therapeutic alliance in schizophrenia has been linked with treatment adherence and outcome, less is known about the clinical correlates of therapeutic alliance. One possible predictor of ability or need for therapeutic alliance in schizophrenia is neurocognition.

Method: Twenty-three participants with SCID-I confirmed diagnoses of schizophrenia or schizoaffective disorder and their therapists were separately administered versions of the Working Alliance Inventory, Short Form (2; WAI-S) after three months of cognitive-behavior therapy. WAI-S totals for clients and therapists were correlated with the Hopkins Verbal Learning Test (HVLT), subtests of the Weschler Intelligence Scale III (WAIS III), the Wisconsin Card Sorting Test and a Continuous Performance Test, all obtained prior to participants beginning therapy.

Results: Poorer performance on the HVLT predicted client report of stronger alliance (r=0.59; p < 0.01). Poorer performance on Block Design subtest of the Weschler Intelligence Test predicted therapist report of weaker alliance (r=0.49; p < 0.05). Client and therapist ratings of therapeutic alliance were positively related but didn’t achieve statistical significance (r=0.39, p=0.07).

Conclusions: More cognitively disabled clients may perceive a stronger alliance whereas therapists may perceive a stronger alliance with more able clients. Client’s abilities may differentially affect therapist and client perception of therapeutic alliance in schizophrenia.

Funding Sources: National Institute of Mental Health, Department of Veteran Affairs, Rehabilitation Research and Development Service

References:

NR645 Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Dose-Ranging Study of Aripiprazole in Patients With Alzheimer’s Dementia Supported by Bristol-Meyers-Squibb and Otsuka Pharmaceutical Co., Ltd

Christopher Breder, M.D., Neurosciences Department, Bristol-Myers Squibb, 5 Research Parkway, Wallingford, CT 06492; Rene Swainik, M.S.C., Ronald N. Marcus, M.D., Susan Kostic, Ph.D., Taro Iwamoto, Ph.D., William H. Carson, Jr., M.D., Robert D. McQuade, Ph.D.

Educational Objectives:
1. To evaluate fixed-dose aripiprazole for the treatment of institutionalized patients with psychotic symptoms associated with Alzheimer’s dementia (AD).

Summary:
Objective: To evaluate fixed-dose aripiprazole for the treatment of institutionalized patients with psychotic symptoms associated with Alzheimer’s dementia (AD).

Methods: This multicenter, double-blind, placebo-controlled trial randomized 487 institutionalized patients with psychotic symptoms associated with AD to treatment with fixed doses of aripiprazole or placebo for 10 weeks. Aripiprazole was dosed at 2, 5 or 10 mg/day. Efficacy assessments included the NPI-NH Psychosis subscale (primary variable) and Total scale, BPRS, CGI, and Cohen-Mansfield Agitation Inventory (CMAI) score.

Results: Aripiprazole-treated patients (10 mg/day) showed significant improvement relative to placebo in the NPI-NH psychosis subscale at endpoint (–6.87 vs –5.13; P=0.013). Other measures where aripiprazole (10 mg/day) showed significant improvements at endpoint included the NPI psychosis response rate (65% vs 50%, P=0.019), changes in CGI Severity (–0.72 vs –0.46, P=0.031) and BPRS total scores (–7.12 vs –4.17, P=0.030). The BPRS Core and CMAI scores improved with both the 10 mg/day and the 5 mg/day dose. The occurrence of EPS-related AEs was 6% with placebo and 7% with aripiprazole.

Conclusions: Aripiprazole treatment resulted in significant improvements in symptoms of psychosis, agitation and clinical global impressions. Aripiprazole was well tolerated in this population.

Funding Sources: Bristol-Myers Squibb Company and Otsuka Pharmaceutical Co., Ltd

References:

NR646 Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Predictors of Readiness to Discharge Among Inpatients With Schizophrenia Supported by Janssen Pharmaceutica and Research Foundation

Andrew Greenspan, M.D., CNS Medical Affairs, Janssen Pharmaceutical, 1125 Trenton-Harbourton Road, Titusville, NJ 08560; Colette Kosik-Gonzalez, M.A., Cynthia Bossie, Ph.D., Young Zhu, Ph.D., Georges Gharabawi, M.D.

Educational Objectives:
1. To identify factors that predict readiness to discharge.

Summary:
Objective: Compare risperidone, quetiapine, and placebo in acutely exacerbated inpatients with schizophrenia for symptom improvement and readiness for hospital discharge.

Methods: In an ongoing double-blind study, inpatients with schizophrenia/schizoaffective disorder with recent exacerbation of psychotic symptoms were randomized to risperidone, quetiapine, or placebo. Assessments included PANSS, CGI-S, HAMD, and a new tool, the Readiness to Discharge Questionnaire (assessing suicidality/homicidality, aggression/impulsivity, ADLs, taking medications independently, delusions/hallucinations, CGI-S, and readiness to discharge [yes/no]). Baseline predictors of readiness to discharge were explored.

Results: Data are available for 194 patients: mean age, 35.4 years (SD 10.2); 67.5% male; mean duration of schizophrenia, 11.2 years (SD 10.1). At baseline, mean PANSS scores were 95.7 (SD 19.4) and mean HAMD scores were 12.0 (SD 6.8). The only significant predictor of readiness to discharge was duration of schizophrenia (longer duration associated with a shorter time until readiness to discharge; P=0.001). There was a consistent increase in the percentage of patients with ≥30% reduction in PANSS total scores over the first 14 days, and a similar increase in...
NR647  Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Cognitive-Behavioral Therapy and Work Outcome in Schizophrenia
Paul H. Lysaker, Psychiatry Department, Roudebush VA, 1481 West 10th Street, Indianapolis, IN 46202; Louanne W. Davis, Psy.D.

Educational Objectives:
At the conclusion of this poster presentation, participants should be able to recognize components and effects of a manualized cognitive-behavioral therapy intervention implemented as an adjunct to vocational rehabilitation.

Summary:
Objective: Many with schizophrenia wish to work, yet enter vocational rehabilitation with expectations of failure. These beliefs represent a barrier to desired levels of function. Cognitive behavior therapy (CBT) has proven to be useful to persons with schizophrenia and could be adapted to enhance vocational outcomes.

Method: Thirty participants with SCID-I confirmed diagnoses of schizophrenia or schizoaffective disorder were randomly assigned to receive a six-month work placement and manualized CBT (n = 15) or a work placement and standard services (n = 15). Hours of work were assessed weekly and work performance was assessed biweekly using the Work Behavior Inventory. Beliefs about self and work were assessed weekly and work performance was assessed biweekly using the Work Behavior Inventory.

Results: Participants randomly assigned to CBT worked equivalent hours to those receiving standard services initially, but by month four they were working significantly more hours (t=1.9; p<.05). CBT participants also demonstrated better work performance during the second half of the program (t=2.0; p<.05) and more hope at five month follow-up, covarying for hope at baseline (f=17.1, p<.0001).

Conclusions: With replication results suggest CBT may assist some with schizophrenia to achieve better work outcomes.

Funding Source(s): Department of Veteran Affairs, Rehabilitation, Research and Development Service

References:

NR648  Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Patients Switched From Olanzapine to Long-Acting Risperidone
Supported by Janssen Pharmacutica and Research Foundation and Johnson & Johnson Pharmaceutical Research and Development
Sally A. Berry, M.D., Medical Affairs, CNS, Janssen Pharmaceutical, 1125 Trenton-Harbourton Road, Titusville, NJ 08560; Ann Clark, Ed Crumbley, B.A., Young Zhu, Ph.D., Robert Lasser, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to describe the safety and efficacy of long-acting injectable risperidone (Risperdal Consta™) in symptomatically stable patients with schizophrenia switched directly from oral olanzapine without a preliminary period of oral risperidone.

Summary:
Objective: To assess the safety and efficacy of switching 50 symptomatically stable patients with schizophrenia directly from olanzapine to long-acting injectable risperidone (Risperdal Consta™) without a preliminary period of oral risperidone.

Methods: After a four-week run-in period during which the patients continued to receive olanzapine, long-acting risperidone (25-50 mg) was given every two weeks for 12 weeks. Concomitant olanzapine was given for the first two of the 12 weeks and then tapered and discontinued during week 3.

Results: Forty patients (80%) completed the study during which the mean dose of olanzapine was 15.2±8.8 mg/d. A clinical response (>20% reduction in PANSS total scores) was achieved by 44% of these stable patients. Mean (±SE) PANSS scores were reduced from 60.4±1.7 to 57.8±2.2 at endpoint. Most frequently reported adverse events were insomnia in eight, rhinitis in five, dizziness in four, and psychosis in four. No clinical adverse events associated with hyperprolactinemia were reported. The patients had a mean weight loss of 0.5 kg (1 lb) during the 12-week trial.

Conclusions: Stable patients who had been treated with olanzapine experienced clinical benefits with no unexpected adverse events when switched directly to long-acting injectable risperidone.

Supported by Johnson & Johnson Pharmaceutical Research and Development, LLC and Janssen Pharmacutica Products, L.P.

References:

NR649  Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Wellness Education and Subjective Experience of Irish Outpatients With Mental Illness
Supported by Eli Lilly and Company
Lucinda V. Scott, M.D., Psychiatry Department, Cork University, Cork University Hospital, Wilton, Cork, Ireland

Educational Objectives:
Participants will be able to discuss the subjective effects of a wellness program among Irish outpatients.
Objective: To examine how the effectiveness of aripiprazole is affected by prior therapy.

Summary:

Objective: To examine how the effectiveness of aripiprazole is affected by prior therapy.

Methods: Outpatients with schizophrenia or schizoaffective disorder for whom an alteration in medication was considered clinically reasonable (N=1,119) were switched to aripiprazole. The effectiveness of aripiprazole therapy was evaluated using the CGI-I scale after 8 weeks. In addition, patients and caregivers were asked to compare aripiprazole therapy to previous medication.

Results: The mean CGI-I scores at endpoint indicated minimal to much improvement with aripiprazole regardless of whether patients were previously receiving olanzapine, risperidone, quetiapine, ziprasidone, typicals, or >1 antipsychotic (CGI-I values of 2.4-3.0). Most patients preferred aripiprazole to previous medication regardless of prior therapy. The proportion of patients who classified aripiprazole as much better than previous medication was 56%, 48%, 49%, 60%, 53%, and 48% among those switched from olanzapine, risperidone, quetiapine, ziprasidone, typicals, and >1 antipsychotic, respectively. Among caregivers, 34%-48% classified aripiprazole therapy as much preferable to the previous one.

Conclusions: In this naturalistic study, improvements were observed after a switch to aripiprazole regardless of prior treatment. In general, patients and caregivers preferred new therapy to the previous one and this preference was not significantly impacted by immediate prior treatment history.

References:

NR651 Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Efficacy of Psychoeducational Materials in Increasing Patient Knowledge of Illness Management and Treatment: The Team Solutions Program Supported by Eli Lilly and Company

Elizabeth Vreeland, M.S.N., Psychiatry Department, UMDNJ University Behavioral Healthcare, 151 Centennial Avenue, Suite 1500, Picseaway, NJ 08854; Shula Minsky, Ed.D., Matthew A. Menza, M.D., Edward Kim, M.D., Philip Yanos, Ph.D., Michael Gara, Ph.D., Lesley A. Allen, Ph.D.

Educational Objectives:
At the conclusion of this session, participants will be aware of the importance of utilizing psychoeducational interventions as an effective illness management intervention in individuals with schizophrenia.

Summary:

Introduction: An accumulating body of evidence indicates that psychosocial interventions provide an important adjunct to the pharmacologic treatment of persons diagnosed with schizophrenia. These interventions have many common elements and are referred to as "illness management" approaches. Illness management is hypothesized to improve outcomes by helping clients to become better educated about the importance of medication and other treatment options and to learn more effective coping skills. This study tested the effectiveness of a psychoeducational, modular program called "Team Solutions."

Methods: Seventy-four subjects who meet DSM-IV diagnostic criteria for schizophrenia or schizoaffective disorder, and attended a day treatment program were randomly assigned to one of two intervention groups: Team Solutions or "treatment as usual." Outcomes were assessed in the following domains: understanding of schizophrenia, medication adherence, program satisfaction, insight, psychiatric symptoms, quality of life, level of functioning, and the use of psychiatric emergency services.

Results: For subjects who participated in the experimental group, significant improvement was observed in knowledge about schizophrenia, p=.04; and in self-concept, p=.04. Moreover, a trend toward improved medication adherence, p=.09; and awareness of mental illness, p=.08 was obtained. Additionally, client satisfaction was very high. Subjects reported a better understanding of mental illness and that they could cope more effectively with daily problems and stress. No significant differences were found in psychiatric symptoms, level of functioning, or the use of psychiatric emergency services.

Conclusions: Findings suggest that subjects who participated in "Team Solutions" learned how to better manage their illness. Findings may not have been as robust given that "treatment as usual" was provided in a university behavioral health care setting that specializes in treating people with severe mental illness. Fur-
their research with more pertinent control conditions is needed across a variety of treatment settings. 

Funding Source(s): An investigator initiated proposal, funded by Eli Lilly

References:


NR652 Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Predominance of Psychiatric-Based Reasons for Antipsychotic Treatment Discontinuation Supported by Eli Lilly and Company
Hong Liu-Seifert, Ph.D., Neuroscience Department, Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285; Bruce J. Kinon, M.D.

Educational Objectives:
At the conclusion of this session, participant should be able to understand the factors that may cause discontinuation from antipsychotic treatment in patients with schizophrenia.

Summary:
Introduction: This research was conducted to better understand the phenomenon of antipsychotic treatment discontinuation and to provide insight into overall treatment effectiveness.

Methods: This was a post hoc, pooled analysis based on four randomized, double-blind clinical trials that had a duration of 24–28 weeks. The 4 studies included 822 olanzapine-treated patients and 805 patients treated with risperidone, quetiapine or ziprasidone.

Results: Adverse events related to worsening in psychiatric symptoms accounted for 50% (100/200) of all adverse events leading to treatment dropouts, with worsening in psychiatric disorder (35/200) and suicide (completed/attempt/ideation, 18/200) being the most frequent events. Most decisions of discontinuation due to lack of efficacy were made based on patient perception (132/164). Clinical rating scales showed patients who discontinued due to lack of efficacy received no relief of their psychiatric symptoms.

Conclusions: This research demonstrated that worsening of underlying psychiatric symptoms as well as patients’ perception of their failure to improve overwhelmingly contribute to treatment discontinuation, which can threaten patient well-being with the morbid consequences of illness exacerbation. Better understanding of what causes discontinuation may provide a strategy to improve patient engagement in long-term therapy and to increase patient access in realizing the goals of an effective treatment.

Funding Source(s): Eli Lilly and Company

References:

NR653 Wednesday, May 5, 12:00 p.m.-2:00 p.m.
A Comprehensive, Retrospective Study of Associations Between Diabetes and Treatment With Risperidone, Olanzapine, Quetiapine, and Conventional Antipsychotics Supported by AstraZeneca Pharmaceuticals
Frank D. Gianfrancesco, Ph.D., Hecon Associates, 9833 Whetstone Drive, Montgomery Village, MD 20886; Ruy-Hua Wang, M.S.

Educational Objectives:
At the conclusion of this session, the participant should be able to: (1) compare the incidence of diabetes among patients receiving quetiapine, risperidone, olanzapine, and conventional antipsychotics for patients with psychosis; and (2) recognize the impact study design has on the risk of diabetes with antipsychotic medications.

Summary:
Objective: Retrospective studies using large patient databases have conflicting findings regarding diabetes risks associated with antipsychotics.

Methods: To assess sensitivity of findings to study design, claims data were analyzed for thousands of psychosis patients both treated and untreated with antipsychotics. Screening for pre-existing diabetes, identification of diabetes with prescription claims only, and requirement of antipsychotic monotherapy represent better control for confounding influences. Diabetes odds ratios for patients treated with risperidone, olanzapine, quetiapine, or conventional antipsychotics versus untreated patients were estimated varying the above criteria. Logistic regression controlled for patient age, sex, type of psychosis, length of observation/treatment, preexisting excess weight, and use of other drugs with diabetogenic effects.

Results: Findings are reported in the Table. Under the weaker study design, all antipsychotics were associated with significantly higher odds of diabetes relative to patients untreated with antipsychotics. Under the stronger study design, relative odds of risperidone and quetiapine declined, becoming statistically insignificant, while those for olanzapine and conventional antipsychotics increased and remained significant.

Conclusions: In database studies, estimated risks of diabetes among antipsychotics are affected by study design. When a more reliable design is used, risks associated with quetiapine and risperidone are not significantly different from those in untreated patients.

Funding Source(s): The research reported here was supported by AstraZeneca Pharmaceutical's LP.

References:

NR654 Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Oral Glucose Tolerance Tests (OGTT) in Patients With Schizophrenia Treated With Antipsychotics Supported by Bristol-Meyers-Squibb
M. de Hert, M.D., UC St. Jozef, Leuvensesteenweg 517, Kotenberg B 3070, Belgium; D. Van Eyck, M.D., L. Hanssens,
Educational Objectives:

At the conclusion of this session, the participant will have an increased awareness of the importance of metabolic consequences of treatment with antipsychotic medication and be introduced to evidence to devise reliable new screening procedures.

Summary:

Introduction: Epidemiological studies have demonstrated related increased risk of diabetes in schizophrenic patients treated with antipsychotics, irrespective of concomitant weight gain.

Method: Extensive metabolic data are being collected in a large cross-sectional naturalistic sample of treated schizophrenic patients, who will be followed prospectively for 1 year. OGTT data will be obtained on 100 patients. Preliminary data on 37 non-diabetic schizophrenic patients, stable on medication (90% on atypical antipsychotics) for at least six months, have already been analyzed.

Results: All patients had normal fasting glucose levels. 23% of OGTT meet the criteria of diabetes and 29% meet the criteria of impaired glucose tolerance. Furthermore, most patients have post-glucose hyperinsulinism and delayed insulin release, sometimes with a tendency to reactive hypoglycemia.

Conclusion: The observed abnormalities in OGTT may be related to early stages of metabolic complications of antipsychotic treatment. Analysis of covariance will be performed with anthropomorphic measures and specific drugs. The prospective nature of the study will identify the predictive value of the observed abnormalities. Subsequently we aim to develop reliable screening procedures for metabolic disorders linked to the use of antipsychotics.

References:


NR655 Wednesday, May 5, 12:00 p.m.-2:00 p.m.

Long-Term Effects of the Solutions for Wellness Program With Irish Outpatients With Mental Illness Supported by Eli Lilly and Company

Catherine P. Noone, M.D., Psychiatry Department, St. Mary's Hospital, Castlebar, Co Mayo, Ireland

Educational Objectives:

At the conclusion of this session, the participant will be able to discuss the long-term effects of the Solutions for Wellness program on weight and BMI in Irish Outpatients.

Summary:

Objective: To evaluate the effect of a long-term wellness education program on weight in Irish outpatients with mental illness.

Method: 120 outpatients (28 M, 92 F) with various DSM-IV diagnoses completed this 12-month, multi-center study. Patients participated in a weekly, hour-long, wellness education class using a modular system that focused on both nutrition and fitness. Patients were taking a variety of psychotropic medications, including antipsychotics (conventional and atypical), mood stabilizers, antidepressants, and tranquillizers. Patients' weights and BMI's were recorded and compared at baseline, six-months, and 12-months (LOCF).

Results: There was a statistically significant decrease in weight from baseline to 6-months (p=.003) and baseline to 12-months (p<.0001). Patients' BMIs decreased significantly from baseline to 12-months (p<.0001). The site with the greatest amount of weight change (n = 10) reported a mean weight loss of 6.6 kg and 8.7 kg at six-months and 12-months, respectively.

Conclusions: This study suggests that a wellness education program can have a positive influence on weight over a long-term period. Significant reductions in weight were observed at the six-month mark and continue to study end. Controlled trials are warranted to further investigate the effect of educational wellness interventions on weight change in patients with mental illness, as well as, what techniques are most successful in implementing such programs.

References:


NR656 Wednesday, May 5, 12:00 p.m.-2:00 p.m.

Social Relationships, Emotional Well-Being, and Working Memory in Schizophrenia

Hao-Yang Tan, M.B., Psychological Medicine, National University of Singapore, 5 Lowe R. Kent Ridge Road, Singapore 119074, Singapore; Moizza Mansoor, M.B., Lisa Y. Chuah, Ph.D., Hao-Yang Tan, M.B., Wei-Chieh Choo, M.B., Calvin Fones, M.D.

Educational Objectives:

At the conclusion of this session, the participant should better understand the underlying emotional and cognitive processes involved in social impairment in schizophrenia.

Summary:

Objective: Social impairment is an important feature of schizophrenia. We investigated, in a sample of Chinese schizophrenia patients, the predictors of overall health-related quality of life (HRQOL), hypothesizing that the social relationships factor would be important. We then explored its relationship with psychopathology, other domains of HRQOL and the neuropsychological domain of working memory.

Methods: Ninety-four schizophrenia patients were assessed using clinical rating scales, HRQOL (the COOP/WONCA charts) and functional activity rating scales. A subgroup of 50 patients underwent further testing using the WHQOL-100 and the n-back working memory test.

Results: Stepwise linear regression analysis showed that schizophrenia HRQOL was independently predicted by dissatisfaction with social relationships, dissatisfaction with emotional well-being and male gender (R2=0.40; F(4, 51)=14.3, p<0.001). Social impairment correlated with longer duration of illness (r = 0.37, p=0.044), severity of PANSS negative symptoms (r=0.69, p=0.001), and poorer emotional well-being (r=0.50, p=0.005). In an a priori regression model, working memory performance and satisfaction with emotional well-being independently predicted satisfaction with social relationships (R2=0.38; F(2, 332)=8.1, p=0.002).

Conclusion: Dissatisfaction with social relationships is an important factor in poorer schizophrenia HRQOL. Processes associated with working memory and emotional well-being may mediate satisfaction with social relationships.

Funding Source(s): National Medical Research Council, Singapore
References:


NR657  Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Validation of the Readiness-to-Discharge Questionnaire for Schizophrenia
Supported by Janssen Pharmaceutica and Research Foundation

Steven G. Potkin, M.D., Department of Psychiatry and Human Behavior, University of California, Irvine, Robert Sprague, Director of Brain Imaging Ctr, Irvine, CA 92697-3960; Andrew Greenspan, M.D., Colette Kosik-Gonzales, M.A., Young Zhu, Ph.D., Georges Gharabawi, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to identify factors on the Readiness to Discharge Questionnaire that are predictive of readiness for discharge.

Summary:

Objective: To validate a Readiness to Discharge Questionnaire (RDQ) for schizophrenia/schizoaffective disorder following admission for an acute exacerbation.

Methods: A RDQ was used to evaluate 149 inpatients across seven sites (US, India, Romania). Patients were assessed at days 2, 4, 8, 10, 12, and 14 by the five-item RDQ, the Clinical Global Impressions-Severity (CGI-S), and a readiness to discharge question. The RDQ items include actively suicidal/homicidal, control of aggression/impulsivity, activities of daily living (ADLs), taking medications independently, and delusions/hallucinations interfering with functioning. Cross tabulation, proportional hazard regression (PHREQ), and factor analytic methods assessed the factors and readiness to discharge.

Results: No cases of actively suicidal/homicidal patients were considered ready for discharge. Multivariate PHREQ model showed that ADLs, taking medications independently, and delusions/hallucinations were significant predictors of readiness to discharge. Control of aggression/impulsivity, taking medications independently, and delusions/hallucinations were three well accounted variables for the principal components in the factor analysis. Results were similar across sites and countries. RDQ items (ADLs P<.05; taking medications independently P<.001; delusions P<.001) were better predictors of the readiness to discharge question than the CGI-S (P=.76).

Conclusions: The data indicate that all factors contribute to readiness to discharge. Research is underway to examine the sensitivity of the RDQ to pharmacological treatment.

Supported by Janssen Pharmaceutica Products, L.P.

References:


NR658  Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Cost-Effectiveness of Long-Acting Risperidone Injection
Supported by Janssen Pharmaceutica and Research Foundation

Marcia Rupnow, Ph.D., Department of Outcomes Research, Janssen Pharmaceutica Products, L.P., 1125 Trenton Harbourton Road, Titusville NJ 08560; Natalie Edwards, M.S.C., Chris Pashos, Ph.D., Marc Botteman, M.S.C., Julie Locklear, Pharm.D., Ronald J. Diamond, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to compare the one-year cost-effectiveness of long-acting risperidone, oral risperidone (RIS), olanzapine (OLA) and haloperidol decanoate (HAL-DEC) for schizophrenia.

Summary:

Objective: To compare the one-year cost-effectiveness of long-acting risperidone, oral risperidone (RIS), olanzapine (OLA) and haloperidol decanoate (HAL-DEC) for schizophrenia.

Methods: A decision tree model was developed to predict rates of compliance, relapse, adverse events, resource utilization, and healthcare costs. Outcomes were expressed as number and duration of relapses per patient per year and total cost per patient per treatment.

Results: The proportion of patients predicted to relapse and require hospitalization within one year was 66% for HAL-DEC, 41% for RIS and OLA, and 26% for long-acting risperidone. The proportion of patients with an exacerbation not requiring hospitalization was 60% for HAL-DEC, 57% for RIS and OLA, and 24% for long-acting risperidone. The mean number of days of relapse requiring hospitalization per patient per year was 28 for HAL-DEC, 18 for RIS and OLA, and 11 for long-acting risperidone. The mean number of days of exacerbation not requiring hospitalization was 8 for HAL-DEC, 5 for RIS and OLA, and 3 for long-acting risperidone. When compared with HAL-DEC, RIS, and OLA, cost savings with long-acting risperidone were $8534, $692, and $1624, respectively.

Conclusion: Predictive modeling suggests that long-acting risperidone is more cost effective than other treatments owing to its lower rates of symptom exacerbation and hospitalization.

Funding Source(s): Supported by Janssen Pharmaceutica Products, L.P.

References:


NR659  Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Assessment and Treatment of Movement Disorders in Schizophrenia: The Vilan Method
Supported by Novartis Pharmaceuticals Corporation

Nikola N. Ilankovic, M.D., Neuropsychiatry Department, Institute of Psychiatry, Pasterova 2, Belgrad 11000, Yugoslavia; Vera I. Ilankovic, Ph.D., Andrew N. Ilankovic, M.D., Lana Marija Ilankovic

References:


Educational Objectives:

At the conclusion of this session, the participants should understand the new method of assessment and treatment of movement disorders in schizophrenia.

Summary:

Purpose: New research of assessment and treatment of psychomotor disturbances by residual schizophrenic patients. Comparison of effects of neurorehabilitation method VILAN and augmentation with CLOZAPINE.


Results: Dominant psychomotor disturbances were: Abnormality of Tonus/100%, Posture and Postural Reflexes/100%, Voluntary movements/96%, Speech/96% and Involuntary Movements/70%. After rehabilitation with VILAN method the reduction of Dyspaxio was for 86%, Disorders of Simultan Movement for 64%, Depressive retardation for 48%, Parkinsonism for 44%, Speech for 32%, Abnormal movements for 24% and Tardive Dyskinesia for 18%. In group with CLOZAPINE the reductions of Psychomotor disturbances in all categories was significantly higher (p<0.01).

Conclusions & Suggestions: 1. The most of patients with Schizophrenia residual type have psychomotor disturbances/movement & speech disorders/2. The adding of Psychomotoric Rehabilitation ans Speech reeducation in treatment of Schizophrenia residual type is obligatory for functional recovery and their Quality of life. 3. The pharmacotherapy augmentation with Clozapine results with higher improvement of psychomotor functionality of patients with Schizophrenia. 4. We propose adding the movements speech disorders to Diagnostic criterias of Schizophrenia res. type.

Funding Source(s): possibly Novartis

References:

NR660 Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Hippocampus and Amygdala Volumes in Bipolar Disorder Spectrum
Elizabeth Licalzi, B.A., Psychiatry Department, Mount Sinai Medical School, One Gustave Levy Place, New York, NY 10029; M. Mehmet Haznedar, M.D., Stefano Pallanti, M.D., David B. Schnur, M.D., Eric Hollander, M.D., Monte S. Buchsbaum, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant will understand the structural volumetric differences of the hippocampus and amygdala and its clinical significance in bipolar disorder.

Summary:

The hippocampus and amygdala, involved in memory and emotion, are affected in bipolar disorder. Previous MRI studies examining the volume of these structures in bipolar patients have been inconsistent. In the current study we examined hippocampus and amygdala volumes of 40 patients with bipolar disorder (17 bipolar type I, 16 cyclothymia, 7 bipolar type II; mean age=42.3) and 36 sex- and age-matched controls (mean age=40.7). MRI axial acquisitions were done with a 1.5 Tesla GE signa 5x system. One researcher, without knowledge of diagnosis, discretely outlined the hippocampus and amygdala on 1.2mm thick consecutive coronal MRI slices. Bipolar spectrum patients were found to have volumetric variations in amygdala and hippocampus (ANOVA, GroupxRegion F=4.98, df=1, p=0.0296). Bipolar spectrum patients had smaller right hippocampi compared to controls (t=2.48, df=74, p=0.0153). In subgroup analysis, the right hippocampus volume was reduced in the cyclothymia group compared to controls (t=3.03, df=50, p=0.0039) and this finding is inversely correlated with the Hamilton Depression Scale total scores (r=−0.55, df=14, p<0.05). In addition, left hippocampus volume of bipolar type I patients inversely correlated to the duration of illness (r=−0.52, df=15, p<0.05).

This research is funded by a grant from Stanley Foundation for Dr. M. M. Haznedar

References:
NR662 Wednesday, May 5, 12:00 p.m.-2:00 p.m.  
Quantification of Functional Changes in Regional Brain Blood Flow Using SPECT
Carlos Mingote, M.D., Psychiatry Department, Hospital 12 de Oct., Va. Andalucia S/N, Madrid 28041, Spain; Sebastian Ruiz, M.D., Rosa Jurado, M.D., Blanca Bolea, M.D., Jorge Vidal, M.D., Elvira Bermudez, M.D., Tomas Palomo, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the main patterns of functional changes of regional brain blood flow detected in PTSD patients and its current role in diagnosis.

Summary:
Objectives: We aimed to determine possible changes in the regional brain blood flow (rCBF) in PTSD using SPECT. Our secondary purpose was to detect and quantify functional changes produced in these patients under emotional activation.
Method: A group of 30 patients was selected using DSM-IV criteria for PTSD plus 12 volunteer controls. All subjects underwent two brain SPECT after the injection of 99m of TC-HMPAO, one under basal conditions and the other under emotional activation using memories of traumatic events. A half quantitative analysis of the brain rCBF in 24 regions, was carried out calculating rates of relative activity against a reference area.
Results: The mean of the differences of cCBF among SPECT showed a decrease in left dorsolateral prefrontal cortex metabolism (p<0.02). Patients with apathy but without depression (n=17) showed a decrease in left orbitofrontal cortex metabolism (p<0.01).
Conclusions: Depression and apathy are related to different neuroanatomical brain circuits involving specific areas of the frontal cortex.

Grant support: With support from 5th EU Framework Program (NEST-DD)

References:

NR663 Wednesday, May 5, 12:00 p.m.-2:00 p.m.  
A PET-Study in Early Alzheimer’s Disease With Apathy or Depression
Sebastian Spirling, M.D., Psychiatry Department, University of Dresden, Elbauer Str. 16, Dresden, SA 01324, Germany; Susanne Lueddecke, Ph.D., Elke Kalbe, Ph.D., Olaf Lenz, M.D., Bettina Beuthien-Baumann, M.D., Karl Herholz, M.D., Viera A. Holthoff, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize neuronal circuits that mediate apathy and depression in early Alzheimer’s disease.

Summary:
Introduction: The following study examines the association between regional changes in cerebral glucose metabolism and the occurrence of clinically relevant symptoms of depression or apathy in patients suffering early Alzheimer’s disease (AD). The study is aimed at identifying brain areas implicated in behavioural disturbances in AD.
Method: Patients with clinically relevant symptoms of depression or apathy as measured by the Neuropsychiatric Inventory (NPI), were recruited from a cohort of 50 patients (mean age 65±8 years, SD:8.8) with probable AD according to NINCDS-ADRDA criteria (MMSE score mean: 26.1, SD:3.3; Clinical Dementia Score CDR mean:0.7, SD:0.5). Regional metabolic changes were measured using positron emission tomography with [18F]fluorodeoxyglucose and the ECAT EXACT HR Plus PET tomograph (Siemens-CTI). Data analysis was performed for between AD and age-matched controls using statistical parametric mapping (SPM99) comparing age-matched patients with and without the behavioural disturbance under study and comparable scores for the remaining behavioural domains. The significant threshold was p<0.05 and corrected p-values are given.
Results: Patients with depression but without apathy (n=10) showed a decrease in left dorsolateral prefrontal cortex metabolism (p<0.02). Patients with apathy but without depression (n=17) showed a decrease in left orbitofrontal cortex metabolism (p<0.01).
Conclusions: Depression and apathy are related to different brain circuits involving specific areas of the frontal cortex.

Funding Source(s): Spanish Government Health System

References:

NR664 Wednesday, May 5, 12:00 p.m.-2:00 p.m.  
fMRI Activation During a Feature-Binding Semantic Task in Schizophrenia
Cheedem H. Kuzu, B.A., OLIN NRC, Institute of Living, 400 Washington Street, Hartford, CT 06106; Paul Rivkin, M.D., Godfrey D. Pearsson, M.D., John Hart, M.D., Vince D. Calhoun, Ph.D., Michael A. Kraut, M.D., Michael A. Yassa, B.A., Michal Assaf, M.D.

Educational Objectives:
At the conclusion of this session, participants should be able to identify differences in brain activation between schizophrenia patients and healthy controls during feature binding and association tasks related to FTD.

Summary:
Introduction: Formal thought disorder (FTD) is a disabling, poorly understood symptom occurring in psychotic syndromes. One hypothesis is that FTD represents impaired semantic pro-
cessing. Recent studies suggest that **object and feature-binding** semantic sub-processes are normally independent, and that positive FTD is associated with abnormal feature-binding.

**Methods:** Using IMRI, seven schizophrenia and ten matched healthy participants were scanned on verbal **feature-binding** and **association** tasks. During the tasks, participants were presented with word pairs and decided if they bound to a third object or were associated, respectively.

**Results:** There were no significant differences in performance between the patients and healthy participants on either task. For the feature-binding compared with the association task, controls activated the following brain areas more than schizophrenia patients: **Left** dorsolateral prefrontal cortex (DLPFC), ventromedial prefrontal cortex, and anterior cingulate gyrus; **Bilateral** inferior frontal gyrus, thalamus, inferior parietal lobule, and medial fusiform gyrus; and **Right** superior parietal lobule (SPL). Schizophrenia patients had greater activation in the left middle temporal gyrus, bilateral SPL, and right DLPFC.

**Conclusions:** Schizophrenia patients showed abnormal brain activation while performing a feature-binding task sensitive to FTD symptoms, albeit with equal performance. Our results outline a possible pathological brain circuit that underlies FTD.

**Funding Sources:** From NIMH to GP & PR

**References:**

**NR665 Wednesday, May 5, 12:00 p.m.-2:00 p.m.**

**Amygdalar and Orbitofrontal Dysfunction in Panic Disorder: An fMRI Study**

David A. Silbersweig, M.D., Psychiatry Department, FNL, 1300 York Avenue F-1302, Box 140, New York, NY 10021; Almut F. Engelen, M.D., Oliver Tuscher, M.D., Hong Pan, Ph.D., Marylene Ciotre, Ph.D., Jack M. Gorman, M.D., Emily Stern, M.D.

**Educational Objectives:**
At the conclusion of this session, the participant should understand the application of functional neuroimaging in conjunction with neuropsychological paradigms to study neural circuit abnormalities in panic disorder.

**Summary:**
Two of the prominent symptoms of panic disorder are panic attacks and anticipatory anxiety. This disorder has not been extensively studied with neuroimaging, and though frontal and limbic changes have been described, its neurobiological substrates are not well understood. We utilized fMRI with a gradient echo EPI sequence and a z-shimming algorithm, to maximize signal in the ventral brain regions of interest, in conjunction with a modified instructed fear/anticipatory anxiety paradigm, to test hypotheses about abnormal ventral frontal and anterior mesotemporal limbic function associated with fear and anxiety in panic disorder. In the context of study hypotheses, results demonstrated increased amygdalar activity in panic (vs. normal) subjects, in the “safe” condition, especially in the later epochs of the experiment. During the anticipated stimulation condition, normal subjects showed increased amygdalar responses in the early epochs whereas patients had decreased activity. Decreased lateral orbitofrontal activation was seen in panic vs. normal subjects in both conditions. The paradoxical amygdalar activation during the instructed safe condition may constitute a neural substrate for the prominent anticipatory anxiety experienced by panic patients. The abnormal orbitofrontal function may contribute to the dysfunctional top-down modulation of amygdalar activity and output (particularly autonomic responses) in these patients.

**Funding Source(s):** NIMH Center Grant 5-P50 MH58911

**References:**

**NR666 Wednesday, May 5, 12:00 p.m.-2:00 p.m.**

**Decrease of DAT Density Using SPET in Patients With First-Episode Schizophrenia**

Jose J. Mateos, D.D.R., Nuclear Medicine Department, Hospital Clinic Barcelona, Villarroel 170, Barcelona 08027, Spain; Francisco Lomena, Ph.D., Eduard Parellada, M.D., Mireia Font, Javier Pavia, Ph.D., Miguel Bernardo, M.D.

**Educational Objectives:**
FP-CIT SPET is a useful tool to detect decrease of striatal DAT density in schizophrenic patients.

**Summary:**
Between 14% and 35% of naïve schizophrenic patients (SCH) develop extrapyramidal symptoms (EPS), far above that of the general population (1%). The introduction of new radiotraers with affinity to striatal DAT has helped diagnose Parkinson disease in early stages. So, it could be interesting to determine if those SCH patients with EPS show a decrease in DAT density similar to that of Parkinson disease patients.

**Objective:** To determine the striatal DAT density assessed with $^{[123]}$I FP-CIT in first-episode naïve SCH patients treated with risperidone and developing EPS.

**Method:** Thirty age-and sex-matched young adults were studied. Twenty were first-episode SCH patients (DSM-IV criteria) and were treated with risperidone; 10 developed EPS (PK), and 10 did not (NonPK). The remaining 10 were healthy subjects. Simpson-Angus (S-A), CGI and PANSS scales were assessed. After $^{[123]}$I FP-CIT SPET, semiquantitative analyses were performed using regular regions of interest (ROIs) located in the caudate, putamen and occipital cortex. For each ROI, striatal-to-occipital ratios were obtained.

**Results:** The striatal-to-occipital ratios were minor in PK and NonPK groups compared to healthy subjects (p<0.001). Females obtained higher binding ratios than males (p<0.001). No correlation was observed between $^{[123]}$I FP-CIT, S-A and clinical scales.

**Conclusion:** First-episode SCH patients treated with risperidone, with or without EPS, have a decreased striatal DAT density assessed with $^{[123]}$I FP-CIT. This alteration could be related to the SCH disease itself or secondary to the antipsychotic treatment. This study was supported by Maraton TV3: Enfermedades Mentales Graves

**References:**
NR667  Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Hippocampus and Brain-Volume Differences in Schizophrenia and Other Psychoses
Antti Tanskanen, M.D., Department of Radiology, University of Oulu, Kajaanintie 50, PO Box 5000, Oulu University 90014, Finland; Juha M. Veljola, Ph.D., Ulla K. Pihllo, M.D., Marianne Haapea, M.S.C., Ed T. Bullmore, M.D., Peter B. Jones, M.D., Matti K. Isohanni, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize hippocampus amygdala and brain volume differences in schizophrenia and other psychoses in population based birth cohort sample, and recognize the effects of potential mediating factors.

Summary:
Objective: To define volume differences of hippocampus, amygdala and other brain regions in patients with schizophrenia or any psychosis, and analyze effects of family history of psychosis, perinatal risk and age at onset of illness.

Methods: All subjects with psychosis from Northern Finland 1966 Birth Cohort were invited for a survey in 1999–2001 including MRI scan of the brain. Brain volumes were measured in 56 subjects with schizophrenia, 26 patients with other psychoses, and in 104 controls.

Results: Smaller total brain and larger cerebrospinal volumes were found in schizophrenia and all psychoses category. Small reduction in hippocampal volume in schizophrenia (2%) and all psychoses (3%) disappeared when adjusted for total brain volume. Mean amygdala volume did not differ from controls. Family history of psychosis or perinatal risk did not have effect in either diagnostic groups compared to controls. However, patients with family history of psychosis had larger hippocampus than patients without. Age at onset of illness had no effect.

Conclusion: Small hippocampal volume reduction in schizophrenia and all psychoses explained by whole brain volume differences in this population based sample. Perinatal events that have been suggested as of etiological importance in structural pathology had no effect.

References:

NR669  Wednesday, May 5, 12:00 p.m.-2:00 p.m.
fMRI of Oddball Processing in Bipolar Illness
Kent A. Kiehl, Ph.D., Psychiatry Department, Hartford Hospital, Olin NRC, 200 Retreat Avenue, Hartford, CT 06106; Michael C. Stevens, Ph.D., Amanda Ortgren, M.A., Kim A. Celone, B.S., Godfrey D. Pearson, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to: (1) identify neural circuits in schizophrenia showing abnormal hemodynamic activity; (2) relate neurofunctionally impaired brain regions to target detection and orienting cognitive processes.

Summary:
Introduction/Hypotheses: Event-related potential (ERP) studies of target detection (i.e., oddball) tasks suggest that bipolar illness patients demonstrate abnormalities in latency and amplitude of the P300 (Muir et al., 1991; Souza et al., 1995). However, the neural systems underlying these abnormalities remain unclear. We hypothesized that cerebellar-thalamic-frontal circuits would be impaired in bipolar illness as demonstrated by fMRI studies of auditory target detection task.

Methods: fMRI data were collected from 13 bipolar patients and 13 matched controls during performance of an auditory oddball target detection task.

Results: Patients with bipolar illness, relative to controls, demonstrated reductions in hemodynamic activity in rostral anterior cingulate, left lateral frontal cortex, thalamus and cerebellum. Excessive activity was observed in bipolar patients in medial temporal lobe (i.e., hippocampus/amygdala) and bilateral occipital cortex.

Discussion: The results support the hypothesis that bipolar illness is associated with abnormalities in cerebellar-thalamic-frontal circuit function. Furthermore, as is found in schizophrenia, the results suggest that bipolar illness may be characterized by impairment in the modulation of neural activity at diverse cerebral sites (i.e., the disconnection hypothesis). It remains to be elucidated if these abnormalities are state-related, and whether they are restricted to psychotic bipolar persons.

References:
Fund in part by a Hartford Hospital Open Competition Award (PI-Kiehl 2003).

References:

NR670 Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Increased Brain Activity After Secretin Administration: An fMRI Study
Supported by Repligen Corporation
Deborah A. Yurgelun-Todd, Ph.D., Department of Neuroimaging, McLean Hospital, 115 Mill Street, Belmont, MA 02478; Staci A. Gruber, Ph.D., Jadwiga Rogowska, Ph.D., Patrice Rioux, Ph.D., Karen Juaregui, Jim Rusche, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participant should recognize the potential effects of secretin administration.

Summary:
Introduction: Neuroimaging studies indicate that the regions in the amygdala responsible for affective processing of visual stimuli are sensitive to pharmacologic manipulation. The amygdala has emerged as one of the most critical areas for ascribing emotional significance to stimuli and influencing affective responsiveness and emotional learning. Recent investigations suggest that secretin, a peptide found in gut and brain tissue, activates gene expression in the central nucleus of the amygdala in rats.

Methods: To elucidate neurophysiological effects of secretin on cortical activation, we applied fMRI techniques to healthy subjects during the viewing of affective faces. We hypothesized that following administration of secretin, controls would show increased BOLD signal change in response to affective stimuli, specifically fearful faces. fMRI scans of 12 adult male subjects were acquired during the presentation of happy, fearful, and neutral faces both before and after an infusion of secretin or placebo.

Results: Within the secretin group, subtraction of the treatment minus the baseline activation during the fear condition yielded significant (p = .001) activation in the right amygdala and a nonsignificant increase in activation in the left amygdala. In contrast, when viewing happy or neutral faces, no significant differences were seen between pre and post infusion within the amygdala. Within the placebo group, no significant differences were detected for any facial affect.

Conclusions: These results, indicating a BOLD signal increase in response to fearful face stimuli, support the hypothesis that secretin alters amygdala responsiveness to affective stimuli. Changes within the amygdala during facial affect processing may be mediated by a variety of neural networks.

Funding Source(s): Repligen Corporation

References:

NR671 Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Prefrontal EEG Cordance Correlates With Anterior Cingulate Perfusion
Supported by Aspect Medical Systems, Inc
Andrew F. Leuchter, M.D., Department of Psychiatry, Neuropsychiatric Institute-UCLA, 760 Westwood Plaza, Room 37-428, Los Angeles, CA 90024-8300; Ian A. Cook, M.D., Scott Greenwald, Ph.D., Tim Kofol

Educational Objectives:

Summary:
Objective: Changes in depression severity have been associated with changes in perfusion of the anterior cingulate. Task activation of the anterior cingulate generates theta power (4–8 Hz) in prefrontal EEG. This work evaluated whether prefrontal EEG theta cordance, a metric that predicts response to antidepressant treatment, would correlate with perfusion of the anterior cingulate.

Methods: PET perfusion values corresponding to Brodmann areas 24 and 32 of the anterior cingulate were extracted from H2 15O PET images recorded during resting baseline and task states. Prefrontal EEG theta cordance was calculated from 35-channel EEG recordings performed simultaneously. Associations were examined between changes from baseline perfusion (ΔPerfusion) and cordance (ΔCordance) during task performance.

Results: Twenty observations were extracted from four subjects. The Pearson Correlation Coefficient between ΔPerfusion and ΔCordance for all subjects pooled was 0.76 (p < 0.01; Rsq = 0.57). Prefrontal EEG theta cordance increased with increasing perfusion.

Conclusions: Prefrontal EEG theta cordance, acquired from the scalp, had a moderately strong association with measured perfusion from the anterior cingulate (i.e., Brodmann areas 24 and 32). This suggests that prefrontal cordance measurements may be useful for monitoring activity of the anterior cingulate cortex. This finding may help to explain the observation that changes in prefrontal EEG theta cordance predict response to antidepressant medication.

Funding Source(s): Aspect Medical Systems, Inc., PHS/National Institute of Mental Health - K08 MH03483 - Drug Sensitivity in Elderly Psychiatry Patients, and NIMH - K02 MH01165 - Enhancing Treatment Outcomes in Depression.

References:

NR672 Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Ventricular Size in Good and Poor Outcome Schizophrenia
Lina S. Shihabuddin, M.D., Department of Psychiatry, Mt. Sinai School of Medicine, One Gustave Levy Place, PET Lab Box 1505, New York, NY 10029; Monte S. Buchsbaum, M.D., Adam M. Brickman, M.A., Randall Newmark, B.A., Michael Dorfman, B.A., Erin A. Hazlett, Ph.D., Kenneth L. Davis, M.D.
Educational Objectives:
At the conclusion of this session, the participant should appreciate ventricular, cortical, and subcortical differences among good and poor outcome patients with schizophrenia and normal controls.

Summary:
Structural MRI was obtained on 54 poor outcome and 52 good outcome patients with schizophrenia, and 42 age- and sex-matched normal controls. The ventricles were traced on every 1.2 mm thick axial slice and volumes of the lateral, anterior, and temporal ventricular regions assessed. Patients with schizophrenia had larger ventricles than normal controls and good outcome patients had larger ventricles than poor outcome patients. The largest effect was for the left temporal horn and poor outcome patients while little volume difference was seen for the anterior horn. Reduction in brain volume of cortex adjacent to individual regions of the ventricles was weakly correlated with white matter but not gray matter content of these areas and restricted to the temporal lobe. These results suggest that more brain tissue reduction is associated with more severe outcome but whether the course of brain tissue reduction is progressive requires longitudinal studies. This is a replication of our previously published CT data on a larger sample with improved imaging techniques.

Funding Source(s): Veterans Administration

References:


NR674 Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Thalamus Size in Good and Poor Outcome Schizophrenia

Adam M. Brickman, M.A., Department of Psychiatry, Brown Medical School, Coro West 3rd Floor, 1 Hopkins Street, Providence, RI 02903; Monte S. Buchsbaum, M.D., Lina S. Shihabuddin, M.D., Randall Newmark, B.A., Jennifer N. Lo, B.A., Serge A. Mitelman, M.D., William M. Byne, M.D.

Educational Objectives:
At the conclusion of this session, the participant should appreciate thalamus size differences among good and poor outcome patients with schizophrenia and normal controls.

Summary:
The thalamus has extensive and reciprocal connections to the striatum and cortex and its association nuclei are importantly involved in maintaining attention and modulation of sensory input. The disturbance of these functions in schizophrenia has implicated the thalamus as a nexus of defective circuits in schizophrenia. In the current study, the size of the thalamus was measured in 106 patients with schizophrenia and 42 matched normal controls using high-resolution magnetic resonance imaging (MRI). Schizophrenia patients were divided into poor-outcome (n=54) and good-outcome (n=52) subgroups based on longitudinal analysis of self-care deficits. The thalamus was manually traced on five axial levels proportionately from dorsal to ventral slices. Further, measurements of frontal lobe and temporal volume were made with a semi-automated program that calculated volume within each Brodmann area. Schizophrenia patients, collapsed across good- and poor-outcome patients, had smaller thalami than normal controls at more ventral levels (F(4,584)=3.47, p=0.008) and poor-outcome patients had significantly smaller ventral thalamus than good-outcome patients (F(4,416)=9.66, p<0.0001) when the two subgroups were compared. Within the schizophrenia patients, thalamus size was positively associated with frontal lobe and temporal lobe volume. Thalamus size was also associated with positive symptom and general psychopathology severity. These findings are consistent with post-mortem and MRI measurement suggesting reduction in volume of the pulvinar nucleus, which occupies a large proportion of the ventral thalamus and which has prominent connections to the temporal lobe. Together with previous analyses from our laboratory, the findings implicate posterior brain circuitry abnormalities in poor functional outcome of schizophrenia.

Funding Source(s): Veterans Administration

References:
1. Byne W, Buchsbaum MS, Kemether E, Hazlett EA, Shinwari A, Mitropoulou V, & Sleier LJ (2001); Magnetic resonance levels. Caudate size was similar among the three groups. These findings suggest that there are distinguishing anatomical features underlying the pathophysiologic differences between good and poor outcome schizophrenia. These anatomical differences may underlie the different course, outcome, and treatment response between these two groups.
imaging of the thalamic mediodorsal nucleus and pulvinar in schizophrenia and schizotypal personality disorder. Archives of General Psychiatry, 58, 133–140.


NR675 Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Cortical Brodmann’s Area Volume Correlations With the Cingulate and Outcome in Schizophrenia
Serge A. Mitelman, M.D., Department of Psychiatry, Mount Sinai School of Medicine, One Gustave Levy Place, Box 1505, New York, NY 10029-6574; Lina S. Shihabuddin, M.D., Adam M. Brickman, M.A., Erin A. Hazlett, Ph.D., Monte S. Buchsbaum, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize differences in cortical volume correlations between patients with schizophrenia and normal comparison subjects, as well as between schizophrenia patients with good and poor outcomes.

Summary:
In this study, we systematically examined the correlations of gray matter volumes between each of the Brodmann’s areas in the cingulate arch and extracingulate cortical areas, and their relationship to outcome in schizophrenia. T1-weighted 1.2-mm-thick MR images were acquired in 37 patients with schizophrenia, divided into poor-outcome (Kraepelinian, n=13) and good-outcome (non-Kraepelinian, n=24) subtypes, and in 37 age- and sex-matched controls. The images were classified into tissue types and assigned to Brodmann’s areas using the Perry’s post-mortem histological atlas. We evaluated the bivariate correlation coefficients for relative gray matter volumes between each cingulate area and all other Brodmann’s areas. Patients with schizophrenia had lower gray matter volume correlations between anterior cingulate and the dorsolateral prefrontal cortices while correlations between anterior cingulate and temporal/parietal/occipital cortices tended to be higher than in normal controls. There was a strong topographic relationship with group differences in anterior cortex related to anterior cingulate and group differences in posterior cortex related to posterior cingulate. Good-outcome and poor-outcome patients displayed significant differences in correlations between anterior cingulate and dorsolateral prefrontal/temporal, between posterior cingulate and primary motor, and between retrosplenial and primary auditory cortices.

Funding Source(s): Mt. Sinai School of Medicine

References:

NR676 Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Psychopathology and Dopamine Transporter Density in Schizophrenia
Chul-Eung Kim, M.D., Psychiatry Department, INHA University, 7-208 3rd Street, Shinheung-Dong, Inchon 400-103, Korea; Jong Hwan Nam, M.D., Myung Hoon Lee, M.D., Pil Gu Lee, M.D., Won Sick Cho, M.D., Seong Jae Pyo

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize, that DAT density in basal ganglia in patients with schizophrenia would be a predicting factor in treatment response.

Summary:
Objectives: Using [123I]IPT-SPECT, we compared between the dopamine transporter(DAT) density of the basal ganglia in first-episode patients with schizophrenia and DAT density in normal control subjects. We investigated the change between DAT density before and after administering olanzapine for four weeks in patients with schizophrenia. We studied correlations between the clinical symptoms of schizophrenia and DAT density.

Methods: Ten patients with schizophrenia and ten healthy control subjects were included in this study. Brief Psychiatric Rating Scale (BPRS) and Montgomery-Asberg Depression Rating Scale(MADRS) were obtained before and after four-week treatment with olanzapine in the schizophrenic group. Nuclear imaging using [123I]IPT-SPECT was obtained in normal control subjects and schizophrenic group before taking olanzapine. After four-week treatment with olanzapine. Nuclear imaging was obtained in schizophrenic group.

Results: No significant difference in DAT density were found between schizophrenic group before treatment and controls. There is significant negative correlation between BPRS total score, withdrawal subscale score after treatment and DAT density before treatment. There is a significant positive correlation between the age of onset and DAT density after treatment and there is significant negative correlation between the duration of illness and DAT density after treatment. There is no correlation between the age of patients and DAT density.

Conclusion: The data of this study suggest that DAT density in basal ganglia in patients with schizophrenia would be a predicting factor in treatment response.

References:

NR677 Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Proton Magnetic Resonance Study in First-Episode Versus Chronic Schizophrenia
Agata Szulc, M.D., Department of Psychiatry, Medical University, Pi. Brodowicza 1, Chorzow 16-070, Poland; Beata Galinska, M.D., Eugeniusz Tarasow, M.D., Wojciech Dzienis, M.D., Bozena Kubas, M.D., Andrzej Czerniakiewicz, M.D., Jeryz Walecki, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to consider some information about neuronal and metabolic abnormalities in brains of schizophrenic patients, which may be comprehensive with neurodevelopmental theory of schizophrenia.
Summary:

Objective: The present study was performed to determine whether there are any differences between chronic and first-episode schizophrenic patients in metabolite levels as measured by 1H MRS.

Method: Localized in vivo proton magnetic resonance spectroscopy (1H MRS) was used to measure metabolic levels in 17 chronic patients (mean duration of illness 9.3 years), 31 first-episode patients with ICD-10 diagnosis of schizophrenia, and 13 healthy controls. Voxel of 8 cm³ were positioned in the left frontal and temporal lobes and the left thalamus. N-acetylaspartate (NAA), choline (Cho), Glx complex (glutamate+glutamine+GABA) to creatine (Cr) and to non-suppressed water signal ratios were analyzed.

Results: We didn’t observe statistically significant differences in metabolite levels between first-episode and chronic patients. Compared with the control group patients demonstrated significantly higher Cho level in the frontal lobe (both groups) and significantly higher Glx level in the temporal lobe (first-episode patients). NAA and Glx levels in the temporal lobe were related with symptoms severity, but not with age, sex and duration of disease.

Conclusions: These results suggest that abnormalities in metabolite levels in frontal and temporal lobes are present at the onset of disease and don’t progress over time. The effect of chronic antipsychotic medication should be considered.

References:


NR678 Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Duration of Untreated Psychosis and MRS Findings in First-Episode Schizophrenia

Beata Galinska, M.D., Psychiatry Department, Medical University, Pl. Brodowicza 1, Choroscz 16-070, Poland; Agata Szulc, M.D., Eugeniusz Tarasow, M.D., Bozena Kubas, M.D., Woyciech Dziens, M.D., Andrzej Czerkiewicz, M.D., Jerzy Walecki, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to consider some information about metabolic abnormalities in brains of first-episode schizophrenic patients.

Summary:

Objective: Previous proton MR studies (1H MRS) have reported abnormalities in metabolite levels in patients with first-episode schizophrenia. Regarding meaning of duration of untreated psychosis the purpose of this study was to determine metabolite changes in short and long DUP groups.

Method: We studied 30 patients (20 male and 10 female, mean age-22.48) with diagnosis of first-episode schizophrenia (ICD-10 and DSM-IV). Their clinical symptoms and cognitive functions were assessed. MR imaging and MR spectroscopy examinations were performed on 1.5 T scanner with single voxel PRESS sequence. Voxel of 2x2x2 cm³ were positioned in the left frontal and temporal lobes and the left thalamus. Metabolites (NAA, Cho, ml, Glx) to creatine ratios as well as the ratios of metabolites to non-suppressed water signal were analyzed.

Results: The median value of DUP was 10 weeks. The long and short DUP groups demonstrated no differences in level of clinical symptoms and cognitive functions. NAA/CR ratio in left frontal lobe was slightly higher in the long DUP group than in short DUP group. No differences in other metabolites levels were found.

Conclusions: The assessed toxic effect of untreated psychosis is not expressed in metabolite abnormalities in first-episode schizophrenic patients.

References:


NR679 Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Craving in Pathological Gambling: An fMRI Study

David N. Crockford, M.D., Psychiatry Department, University of Calgary, 1403 29th Street NW #203, Calgary, AB T2N 2T9, Canada; Bradley Goodyear, Ph.D., Hermeno Tavares, Ph.D., Jerome P. Quickfall, M.D., Jodi Edwards, M.A., Nady El-Guebaly, M.D.

Educational Objectives:

At the conclusion of this session, the participant should recognize that specifically activated brain regions may underlie the subjective craving for pathological gambling and understand that selective priming of salient contextual memories may lead to the persistence of pathological gambling.

Summary:

Objective: Functional Magnetic Resonance Imaging (fMRI) has identified specific brain regions activated with cravings in chemically addicted patients. Identifying underlying neurobiologic factors to pathological gambling could help develop novel treatments for the disorder, but also serve to study the gamut of addictive disorders without the potential confound of substance intake.

Method: 10 DSM-IV pathological gamblers were compared to 10 matched healthy controls via fMRI of the brain. Using a repeated block design, participants were exposed to a nature video, alternating with a video designed to induce craving for gambling or a gambling task.

Results: Male pathological gamblers displayed consistent and significant increased blood flow to the right dorsolateral and ventrolateral prefrontal cortices, bilateral medial temporal structures (hippocampal and parahippocampal gyrus), and bilateral visual and dorsal parietal cortices compared to control subjects. The differential pattern of activation for pathological gamblers was associated with a significantly different mean craving response for gambling.

Conclusions: Similar to findings with substance use disorders, male pathological gamblers displayed brain activation in regions associated with the experience and application of contextual memory during subjective craving for gambling. These results suggest that selective priming of salient memory pathways may underlie the persistence of pathological gambling.

Funding Source(s): Alberta Gaming Research Institute

References:

to identify the neuroanatomic pathways involved in catatonia, as tonic posturing are well described. Its neurochemistry and treatment response are well described (Lorazepam and ECT). It is present in a small, circumscribed population of patients. It is diagnostically heterogeneous in DSM-IV but psychopathologically homogeneous. Catatonia can be seen, identified, studied, mapped, treated, and can translate the other forms of psychosis. There is no single focal lesion responsible for catatonia. It is not focal/localized lesion or region but rather a loop, a neural circuit. The Rosetta Stone argued that in order to translate Egyptian hieroglyphics complete sentences and context were required because translation of individual hieroglyphics did not lead to an understanding of the language.

This new understanding of psychosis pinpoints the pathway dysfunction as outlined by Dr. Northoff. This poster presentation will illustrate the neuroanatomic model and its transposition to a three-dimensional floor plan.

Funding Source(s): The Neuroscience Alliance

References:

NR682 Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Psychosocial Rehabilitation Centers and Psychiatric Hospitalization Rates
Fabio G. Souza, M.D., Department of Psychiatry, Fed. Universidaed of Ceara, Manoel Jesuino, 974-Varjota, Fortaleza Ceara, CE 60175 270, Brazil; Raimundo A.B. Aquino, M.S., Valeria B. Souza, M.P.H., Carolina V. Aquiar, M.D., Cristiana M. Moraes, M.D., Regia M.G. Ramos, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to understand the CAPS (Centro de Atenção Psicossocial) structure and recognize their effective role in the reduction of hospitalization rate in Brazil.

Summary:
Objective: This study aims to evaluate the impact of Psychosocial Rehabilitation Centers (Centro de Atenção Psicossocial - CAPS) in psychiatric hospitalizations in five Brazilian cities where they were implemented.

Methodology: Descriptive data on psychiatric hospitalization authorization from 1995 to 2001 were analyzed taking as reference two years before and two years after the implementation of CAPS. Demographic (sex, age), clinical (diagnosis, duration of hospitalization) and economic data were collected.

Results: An important reduction in the hospitalization rate (36.72%) was observed after CAPS were implanted. This reduction was higher in female (45, 17%) than in male (29.67%). There was a reduction in the admissions of all mental disorders after CAPS: schizophrenia and schizophrenic spectrum disorder (19%); mental disorders related to chemical substances (9.1%); affective disorders (26, 19%); non-specified mental disorders (100%). The hospitalization time was similar in both periods: 30.5 days before CAPS and 30.9 days after CAPS. A reduction of 23% in the expenses with psychiatric hospitalization was observed.

Conclusion: These results suggest that CAPS are important services in the substitution of in-patient for out-patient treatment. Thus helping the implementation of mental reform in Brazil.

References:
NR683 Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Catatonia in Mania and Schizophrenia: Symptom Pattern and Treatment Response
Joseph W. Lee, M.D., Department of Psychiatry, Graylands Hospital, Brockway Road Mt. Claremont, Perth, WA 6010, Australia

Educational Objectives:
- At the conclusion of this session, the participant should be able to recognize that acute catatonia in mania and schizophrenia differ in symptom patterns, catatonic subtypes, and responses to benzodiazepines.

Summary:
- Objective: To examine if acute catatonia in mania and schizophrenia differ in symptom patterns, catatonic subtypes, and responses to benzodiazepines.
- Methods: 126 patients with catatonia requiring psychiatric intensive care were prospectively identified with their catatonie (excited/retarded) subtypes determined based on research criteria. Twenty episodes had mania (16 pure, four mixed) and 43 schizophrenia, all treated with benzodiazepines. Catatonic symptoms were assessed using the Bush-Francis Catatonia Rating Scale (BFCRS). Presence of the four catatonic factors/sub-syndromes—(1) cataleptic malignant syndrome, (2) abnormal involuntary movements/mannerisms, (3) disturbance of volition/catalepsy, (4) cataleptic inhibition—was determined based on equivalent symptoms on the BFCRS supplemented by a chart review for relevant symptoms. Patients with manic catatonia and schizophrenia were compared noting their symptom patterns, catatonic subtypes, and responses to benzodiazepines.
- Results: Manic catatonia manifested predominantly in the excited form, associated with symptom factor 1 and 2, and schizophrenic catatonia significantly more frequently in the retarded form, associated with factor 3 and 4. Manic catatonia had a higher response rate to benzodiazepines (12/16 pure mania, 75%) compared with schizophrenic catatonia (26/43, 61%). In both groups, episodes with intense catatonic excitement tended to respond poorly to benzodiazepines.
- Conclusions: Acute catatonia in mania and schizophrenia differ in symptom patterns, catatonic subtypes, and responses to benzodiazepines.

References:

NR684 Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Rating Scale for NMS
Adeeb E. Yacoub, M.D., Psychiatry Department, Stony Brook University Hospital, HSC T10 Rm 202, Stony Brook, NY 11794-8101; Izchak Kohen, M.D., Angel Caraballo, M.D., Andrew J. Francis, M.D.

Educational Objectives:
- At the conclusion of this session, the participant should recognize and quantify severity and clinical improvement of neuroleptic malignant syndrome using a rating scale.

Summary:
- Objective: Neuroleptic malignant syndrome (NMS) is a rare reaction to antipsychotic medications, characterized by extrapyramidal signs, fever, autonomic disturbance, and laboratory findings. NMS occurs with both conventional and atypical agents. We devised a comprehensive rating scale to facilitate recognition and quantify both severity and clinical improvement.
- Method: After literature review of NMS, a 23-item [max score = 112] anchored severity scale was devised. Scale items include five motor, two behavioral, 10 autonomic, and six laboratory indices of NMS. As NMS is rare, initial data were from retrospective daily ratings on records from 15 episodes meeting full DSM-IV [N=7] or Caroff-Mann [N=8] criteria on the first day of NMS.
- Results: Initial scores [±SE] for the 15 episodes were 34.9 ± 3.7 at presentation, and subsequent daily means were 24.3 ± 2.1, 17.2 ± 2.7, 11.9 ± 2.7, and 7.7 ± 2.5 [P<.01]. Caroff-Mann cases scored higher [P<.05], and the four symptom domains improved in parallel. Initial severity scores did not predict rate of improvement.
- Conclusion: The scale appeared sensitive to clinical improvement. As recent reports show NMS continues to appear with atypical antipsychotics, recognition and prompt treatment will be facilitated by prospective use of a systematic rating scale.

References:

NR685 Wednesday, May 5, 12:00 p.m.-2:00 p.m.
Diagnostic Validity of the Assessment Scales for Depression in Schizophrenia
Sung-Wan Kim, M.D., Psychiatry Department, Chonnam National University, 5 Hack-Dong, Dong-Ku, Kwang-Ju 201-746, Korea; Su-Jung Kim, M.D., Bo-Hyun Yoon, M.D., Michael Y. Hwang, M.D., Jin-Sang Yoon, M.D.

Educational Objectives:
- At the conclusion of this session, participants will become familiar with the assessment scales for depression in patients with schizophrenia and be able to utilize appropriate assessment in clinical practice.

Summary:
- Objective: The comorbid depression in schizophrenia is an important clinical factor in treatment and prognosis. This study aimed to examine diagnostic validity of four assessment scales for depression in schizophrenia.
- Methods: 84 inpatients meeting the DSM-IV criteria for schizophrenia were assessed for depression by DSM-IV criteria for major depressive episode. The Positive and Negative Syndrome Scale (PANSS) and Simpson-Angus Rating Scale (SARS) were utilized to differentiate depression from negative symptoms and EPS-related depressive phenomena. The four widely used depression scales were administered: (1) Calgary Depression Scale for Schizophrenia (CDSS); (2) Beck Depression Inventory (BDI); (3) Hamilton Depression Scale (HAM-D); and (4) depression subscale of the PANSS (PANSS-D).
Results: 32 patients (38%) were diagnosed as having comorbid major depressive disorder. Areas Under Receiver Operating Characteristic (AUROC) curve of the CDSS, PANSS-D, HAM-D, and BDI against DSM-IV depression was 0.94, 0.90, 0.89, and 0.81 respectively. AUROC curve of CDSS showed significantly greater correlation than that of BDI (p<0.005), and higher correlation trend than that of HAM-D or PANSS-D (p<0.1). No significant differences in negative symptom subscale of the PANSS and SARS were noted between depressive and non-depressive subgroups.

Conclusion: The CDSS may provide most valid assessment tool for depression in schizophrenia.

References:

NR686 Wednesday, May 5, 3:00 p.m.-5:00 p.m.
Risk of Committing Suicide in 261 Attempted Suicides: A 30-Year Follow-Up

Heinz Katschnig, M.D., L. Boltzmann Institute, Spitalgasse 11, Vienna A-1090, Austria; Bettina Bankier, M.D., Marion Freidl, D.D.R., Alexander Hanika, M.A., Monika Krautgartner, M.D., Michael Scherer, Peter P. Sint

Educational Objectives:
At the conclusion of this session, the participant should have raised awareness for risk factors for committing suicide in the long-term after attempted suicide.

Summary:
Background: Attempted suicide is usually regarded as a precursor of committed suicide. However, long-term follow-up data are scarce.

Method: In 1971, when all attempted suicides in the city of Vienna (1.7 million inhabitants) were referred to a central hospital ward, a representative one-in-four sample (N=261, 96%; had a diagnosis of reactive depression (ICD-8)) was selected for a prospective actuarial follow-up study.

Results: 30 years later the fate could be cleared for 231 (88.5%) persons; 128 (49.0%) were still alive, and 103 (39.5%) had died. 22 patients (8.4% of the original population) had committed suicide, 7 (2.7%) had died from an unclear cause, and 74 (29.5%) from a natural cause. While the actual number of completed suicides was rather small, the suicide risk was 10 times higher than expected in a matched group of the general population. Two thirds of suicides had occurred in the first ten years of the follow-up period. The best predictors for committing suicide were a repeated attempt already at baseline and a non-conflict motive, usually a definite loss.

Discussion: The data suggest to pay special attention to persons with repeated attempts and experiencing a definite loss, when trying to prevent suicide in persons who attempt suicide.

References:

NR687 Wednesday, May 5, 3:00 p.m.-5:00 p.m.
5-HTT Polymorphism and Family History of Suicide Behavior

Marco A. Romano-Silva, Ph.D., Pharmacology Department, Federal University, Antonio Carlos 6627-UFMG-ICB, Belo Horizonte, MG 31270-901, Brazil; Humberto Correa, M.S.C., Ana C. Campi-Azevedo, M.S.C., Wolanga Boson, M.S.C., Frico da Costa, M.S.C., Luiz A. de Marco, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize that genetic transmission of suicidal behavior is complex and multivariated.

Summary:
Objective: There is compelling evidence that a serotonergic dysfunction may play a major role in suicide behavior and it has also been demonstrated that suicide is, at least partially, genetically determined. Thus, the serotonin-related genes are the major candidates. Previously a functional polymorphism in the promoter region of the serotonin transporter gene (5-HTTLPR) was identified and the presence of the short allele (S) was found to be associated with a lower level of expression of the gene and lower levels of 5-HT uptake when compared to the long allele (L). The purpose of this study was to evaluate the association between family suicide behavior history and probands’ suicide attempt history, suicide attempt characteristics and 5-HTTLPR genotype.

Method: We genotyped 237 probands (major depressed or schizophrenic patients) and used a semi-structured interview to determine probands’ suicide attempt characteristics and first and second degree suicidal behavior.

Results: An association between suicidal family history and proband’s suicide attempt but not with suicide attempt characteristics and probands genotype was found.

Conclusion: Our results suggest that multiple biological and environmental factors underlie familial transmission of suicidal behavior.

References:

NR688 Wednesday, May 5, 3:00 p.m.-5:00 p.m.
TPH Polymorphism and Suicidal Behavior in Brazil

Marco A. Romano-Silva, Ph.D., Pharmacology Department, Federal University, Antonio Carlos 6627-UFMG-ICB, Belo Horizonte, MG 31270-901, Brazil; Melissa Machado, M.S.C., Humberto Correa, M.S.C., Wolanga Boson, M.S.C., Luiz A. de Marco, Ph.D., Frico da Costa, M.S.C.

Educational Objectives:
At the conclusion of this session, the participant should recognize the importance of genetic factor in suicide behavior.

Summary:
Objective: Central serotonergic dysfunction and genetic factors are associated with suicidal behavior in psychiatric patients. The gene that codes for tryptophan hydroxylase (TPH), the rate-limiting enzyme in the biosynthesis of serotonin, is a major candidate. The goal of this study was to examine the association between a polymorphism in the intron 7 of this gene (A218C) and suicidal behavior in a Brazilian sample of psychiatric patients.
Methods: We genotyped 279 subjects. They were schizophrenic (n = 99), major depressed (n = 80), or alcoholic (n = 40), which diagnosis was conducted using a structured instrument (MINI-PLUS) according DSM-IV criteria, and 60 healthy controls. Patients were assessed as regard of their suicide history by means of a semi-structured instrument.

Results: The genotypes (AA, AC, CC) were not statistically different across individuals following diagnosis ($\chi^2 = 1.7, df = 6, p = 0.94$). The genotype was also not associated with the suicide attempt history ($\chi^2 = 1.59, df = 2, p = 0.45$) nor with suicide attempt characteristics in suicide attempter patients.

Conclusion: The authors conclude that the A218C polymorphism of the TPH gene was not a susceptibility factor for suicidal behavior in this group of psychiatric patients.

References:

NR690 Wednesday, May 5, 03:00 p.m.-2:00 p.m.
Time Spent Ill With Bipolar Disorder
Russell T. Joffe, M.D., Department of Psychiatry, New Jersey Medical School, 185 South Orange Avenue, MSB C671, Newark, NJ 07103; Glenda M. MacQueen, M.D., Michael Marriott, Ph.D., L. Trevor Young, M.D.

Educational Objectives:
At the conclusion of this session, the participant should understand the substantial amount of time that patients with bipolar disorders spend ill, especially with minor or subsyndromal symptomatology.

Summary:
There is a recent appreciation that patients with bipolar disorder spend substantial periods of time ill with minor, subsyndromal as well as full-blown manic and depressive symptoms. This study examined time spent ill in a cohort of well characterized bipolar I or bipolar II patients followed prospectively for an average of three years. Detailed life charting data were obtained from 138 patients. Mood states were characterized as euthymic, subsyndromal, minor, or major affective episodes based on rigorous criteria. Patients in the total sample within each bipolar subtype spent approximately half of their time euthymic. The remainder of the time was spent in varying mood states, with the majority of the time spent with minor and subsyndromal symptoms. Bipolar I patients differ from bipolar II patients with significantly more time spent with manic symptoms of all types. The conclusion from this study is that patients with bipolar disorder spend a substantial proportion of the time ill with symptoms of varying severity. This should guide strategies for mood stabilization and bipolar disorder.

References:

NR689 Wednesday, May 5, 3:00 p.m.-5:00 p.m.
Suicide Ideas and Attempts in the General Population of Six European Countries
Josep M. Haro, M.D., Sant Joan de Deu - SSM, Dr. Antoni Pujades, 42, Sant Boi de llobre 08830, Spain; Immaculada Luque, Ron de Graaf, M.D., Jean-Pierre Lepine, Ph.D., Tery Brugha, Maria D. Bernal, B.A.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to identify which mental disorders are the most prevalent in individuals with suicide thoughts in the European population.

Summary:
Objective: To evaluate the frequency of suicide ideas and attempts in the general population of six European countries and its relationship with the presence of mental disorders.

Methodology: This report is part of the European Study of the Epidemiology of Mental Disorders, a cross-sectional personal interview survey conducted in a representative sample of non-institutionalised population older than 18 in Belgium, France, Germany, Italy, the Netherlands, and Spain. Total sample was 21,425 individuals. Response rate was 61.2%. Mental health and suicidality was assessed using the Composite International Diagnostic Interview (CIDI-2000).

Results: Approximately seven percent (1568 individuals) of the population had thought about committing suicide at least once in their lifetime. Of those, 31.1% has made a plan and 26.2% had made a suicide attempt. A logistic regression model showed that females (OR=1.3, p<0.001) were at higher risk. Major depression (OR=3.9, p<0.001), post-traumatic stress disorder (OR=2.2) and dysthymia (OR=2.0, p<0.001) were the mental disorders with higher odds ratio of suicide thoughts. Major depression (OR=5.6, p<0.001), alcohol abuse (OR=2.5, p<0.001) and GAD (OR=2.1, p<0.001) were the disorders with higher association to suicide attempts.

Conclusions: Approximately one fourth of individuals that think about suicide make an attempt. Having a mental disorder is the main risk factor.

Funding Source(s): European Commission (QLG5-CT-1999-01042) Ministerio de Sanidad y Consumo (F1500/28-01) Ministerio de Ciencia Y Tecnología (SAF 2000-158-CE)

References:
Summary:

Objective: Lithium is considered a standard treatment for prophylaxis in bipolar disorder. Appropriate blood lithium levels for maintenance have been reported to be between 0.8 and 1.0 mmol/L. Efficacy of olanzapine versus lithium subgroups, based on blood levels, has previously not been reported.

Methods: This 52-week, randomized, parallel, double-blind study compared bipolar relapse on flexibly-dosed lithium or olanzapine. For this analysis, we defined two post-hoc lithium subgroups. Lower level group (LLG) comprising subjects with mean lithium levels ≤0.8 mEq/L and Higher level group (HLG) comprising subjects with mean lithium levels >0.8 mEq/L.

Results: The olanzapine treatment group had a greater time to relapse into mania or depression (YMRS total score >15 or and HAMD-21 total score >15 or and hospitalization for mania or depression) compared to the HLG (p=.014) but not to the LLG. The olanzapine treatment group had lower rates of manic relapse based on hospitalization for relapse and/or symptomatic rating scale criteria than both lithium treatment groups (olanzapine 14.7% vs. LLG 30.5%; p=.002 and HLG 32.9%; p<.001).

Conclusions: The olanzapine-treated patients had statistically significant lower rates of manic relapse than lithium treated patients, irrespective of lithium level.

Funding Source: Eli Lilly and Company

References:

NR692 Wednesday, May 5, 3:00 p.m.-5:00 p.m.
Prevalence of Bipolar Disorder in a National Managed-Care Health Plan Supported by Bristol-Meyers-Squibb
Carolyn R. Harley, Ph.D., MN002-0258, Ingenix Incorporated, 12125 Technology Drive, Eden Prairie, MN 55344; Robert M.A. Hirschfeld, M.D., Hong Li, Ph.D., Gilbert J. L'Italiano, Ph.D., Alexander M. Walker, M.D., William H. Carson, Jr., M.D.

Educational Objectives:
At the end of the session, audience will understand the prevalence and key comorbidities among patients of bipolar disorder in a large U.S. privately insured program.

Summary:
Introduction: Despite significant financial burden of bipolar disorder, prevalence of bipolar disorder, as well as comorbidities, in the privately insured population has not been reported.

Objectives: To estimate treated prevalence and key comorbidities of bipolar disorder in a large U.S. commercial health plan and to assess common comorbidities.

Methods: Bipolar disorder was identified using ICD-9-CM diagnosis codes (296.0x, 296.1x, 296.4x–296.7x) on insurance claims for medical services. Average annual prevalence was calculated for 1999–2002. Diabetes was identified using diagnosis code 250.xx. Common diagnoses were measured based on frequency of occurrence on medical claims.

Results: Annual prevalence of treated bipolar disorder was 262 per 100,000 enrollees (0.26%). Prevalence of treated diabetes among these bipolar disorder patients was 68 per 1,000 (6.80%). General symptoms (780.xx) was the most frequent comorbidity followed by neurotic disorder (300.xx) and essential hypertension (401.xx). Diabetes was the 17th most common diagnosis.

Discussion: Prevalence of bipolar disorder was lower than national estimates. Diabetes prevalence within the bipolar disorder population was also lower than published data. These findings may reflect a healthier, insured, working-aged population, misdiagnosis, or under-diagnosis of bipolar disorder, and frequency of medical services.

Funding Source(s): Bristol Meyers Squibb

References:

NR693 Wednesday, May 5, 3:00 p.m.-5:00 p.m.
The Bipolar Spectrum in Cluster Headache Patients Supported by Abbott Laboratories
Lawrence Robbins, M.D., Robbins Headache Clinic, 1535 Lake Cook Road, Suite 506, Northbrook, FL 60062; Trupti B. Gokani, M.D.

Educational Objectives:
The participant should be able to recognize cluster headache, and be aware of the increased incidence of bipolar illness among both migraine and cluster patients.

Summary:
Objective and Introduction: The purpose of this study was to determine the incidence of the bipolar spectrum in a large number of cluster headache patients. Previous research has revealed an increase in bipolarity among migraine patients. One previous study of 1000 migraineurs indicated that 8.6% were bipolar.

Methods: Consecutive cluster headache patients, seen over a period of 17 years, were evaluated. The age range was 20 to 78, with an average age of 49. There were 170 men and 105 women. Chart review, as well as interviews with patients and families, was accomplished by the treating neurologist. Lifetime prevalence of bipolar was assessed. Bipolar illness was defined according to DSM-IV. Inclusion criteria were: age 20 or older, and a history of cluster headache as defined by the International Headache Society Criteria.

Results: Of the 275 cluster patients, 134 had episodic cluster, and 141 were chronic cluster sufferers. Episodic cluster: 8 pts(6%) fit the bipolar spectrum. One patient was bipolar I, four were bipolar II, 2 were cyclothymic, while 1 was bipolar NOS. Chronic cluster: 10 pts(7%) were bipolar, two were bipolar I, two bipolar II, four cyclothymic, while two were bipolar NOS. Combined: 18/275 pts(6.5%) were bipolar. 1.1% were bipolar 1, 2.2% bipolar II, 2.2% cyclothymic, and 1.1% bipolar NOS.

Conclusion: This study indicates that, as with migraine, bipolar is seen with an increased frequency among cluster pts.. Certain medications, such as sodium valproates, may be beneficial in treating both illnesses.

This study was funded by a grant from Abbott Laboratories.

References:

NR694 Wednesday, May 5, 3:00 p.m.-5:00 p.m.
Mood, Lability, Temperament, and Mood Disorders
Franco Benazzi, M.D., Department of Psychiatry, Forli National Health Service, Via Pozzotto 17, Cervia Ra 48015, Italy
Educational Objectives:
At the conclusion of this session, the participant should be able to diagnose mood lability temperament and have insight into its impact on mood disorders.

Summary:
Objective: Study aim was to test impact of temperamental mood lability on bipolar-II (BP-II) and major depressive disorder (MDD).
Method: Consecutive 89 BP-II and 89 MDD outpatients, presenting for major depressive episode (MDE) treatment, were interviewed by Structured Clinical Interview for DSM-IV (SCID-CV). Hypomaniac symptoms during MDE were systematically assessed off psychoactive drugs. Kräepelin's basic definition of temperamental mood lability (i.e., frequent up and down fluctuations of mood between the episode since young age) was followed.
Results: TML was present in 56/89 (62.9%) BP-II, and in 30/89 (33.7%) MDD (p=0.000). BP-II with TML, versus BP-II without TML, had significantly lower age at onset, more recurrences, and more hypomanic symptoms during the MDE. Bipolar family history was not significantly different. MDD with TML, versus MDD without TML, had significantly more psychotic features and less axis I comorbidity. Comparisons between BP-II and MDD with TML, on the variables found significantly different in the previous analyses, found that almost all the variables were significantly different.
Conclusion: TML could be a quicker and simple screening tool for BP-II. Its association with more recurrences and depressive mixed states in BP-II (but not in MDD), make the course of this illness and its treatment more complex.

References:

NR695 Wednesday, May 5, 3:00 p.m.-5:00 p.m.
Depressive Mixed State and Course of Mood Disorders
Franco Benazzi, M.D., Department of Psychiatry, Forli National Health Service, Via Pozzetto 17, Cervia Ra 48015, Italy
Educational Objectives:
At the conclusion of this session, the participant should be able to diagnose depressive mixed state and have insight into its relation to course of mood disorders.

Summary:
Objective: Kraepelin's observed, in an inpatient sample, that depressive mixed state (DMX), i.e., a combination of hypo-maniac and depressive symptoms during the same episode, was related to number of episodes and duration of manic-depressive illness. Study aim was to test Kraepelin's observations in a different sample.
Method: Consecutive 563 major depressive episode (MDE) outpatients (320 bipolar-II, 243 major depressive disorder) were interviewed (off psychoactive drugs) by Structured Clinical Interview for DSM-IV (SCID-CV) in private practice. DMX was defined as MDE plus three or more combined hypomaniac symptoms (Akiskal and Benazzi 2003). Kraepelin's agitated depression and depression with racing thoughts were also tested. Logistic regression was used to study associations.
Results: DMX was present in 49.5%. Multivariate regression of DMX versus MDE recurrences and duration of illness, controlled for age, found strong and significant association only between DMX and duration of illness. Same associations were found between agitated depression and duration of illness (but not in depression with racing thoughts).
Conclusion: At the conclusion of this session, the participant should be able to diagnose depressive mixed state and have insight into its impact on mood disorders.

References:

NR696 Wednesday, May 5, 3:00 p.m.-5:00 p.m.
Testing the DSM-IV Hypomania Definition
Franco Benazzi, M.D., Department of Psychiatry, Forli National Health Service, Via Pozzetto 17, Cervia Ra 48015, Italy
Educational Objectives:
At the conclusion of this session, the participant should be able to diagnose bipolar II disorder and have better insight of symptoms.

Summary:
Objective: DSM-IV definition of hypomania in bipolar-II disorder (BP-II) has yet to show its validity. Study aim was to find factor structure of hypomania by using DSM-IV symptoms, and to assess DSM-IV definition of hypomania.
Method: Consecutive 197 BP-II remitted outpatients were interviewed by Structured Clinical Interview for DSM-IV (SCID-CV) in a private practice, assessing symptoms more common during past hypomaniac episodes. Factor structure of hypomania was studied by principal component factor analysis (STATA 7).
Results: Almost all patients reported overactivity (increased goal-directed activity) during hypomania, and less commonly elevated mood. Overactivity plus three or more symptoms identified 89.3% of DSM-IV BP-II. Factor analysis found three factors: Factor 1 included racing thoughts, Factor 2 included elevated mood, and Factor 3 included overactivity. Elevated mood was correlated only with two of the nine DSM-IV hypomaniac symptoms.
Conclusion: The three domains structure of hypomania by Kräepelin (i.e., increased mood, thought, activity) was found in DSM-IV definition of hypomania. An upgrader of overactivity to at least a priority level similar to mood change was supported by its high frequency, its utility to diagnose BP-II, and by factor analysis showing that elevated mood correlated with few symptoms and that only one factor included elevated mood.

References:

NR697 Wednesday, May 5, 3:00 p.m.-5:00 p.m.
HPA and HPT Axis Dysfunction in Depression: Dopaminergic and Noradrenergic Correlates
Fabrice Duval, M.D., Department of Psychiatry, Centre Hospitalier, 27 Rue du 4ème RSM, Rouffach 68250, France; Marie Claude Mokrani, Ph.D., Jose Monreal, M.D., Said Fattah, M.D., Jean-Paul Macher, M.D.
NR699 Wednesday, May 5, 3:00 p.m.-5:00 p.m.
Defining Remission on the Montgomery-Asberg Depression Rating Scale
Mark Zimmerman, M.D., Department of Psychiatry, Rhode Island Hospital, 235 Plain Street, Suite 501, Providence, RI 02905; Iwona Chelminski, Ph.D., Michael A. Posternak, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to describe the cutoffs on the Montgomery-Asberg Depression Rating Scale corresponding to the DSM-IV definition of remission.

Summary:
Background: In antidepressant efficacy trials it is common to define treatment remission as a score below a cutoff on symptom severity measures. No consensus has emerged regarding an appropriate cutoff for defining remission on the Montgomery-Asberg Depression Rating Scale (MADRS). The goal of the present study was to establish an empirically based cutoff on the MADRS for defining remission.

Methods: Three hundred and three depressed psychiatric outpatients were rated on the Standardized Clinical Outcome Rating for Depression, an index of DSM-IV remission status, the MADRS, and the Global Assessment of Functioning (GAF) scale. We examined the sensitivity, specificity and overall classification rate of the MADRS for identifying a broad and narrow interpretation of the DSM-IV definition of remission, and the association between the breadth of the definition of remission and psychosocial functioning.

Results: Based on a narrow definition of remission, which requires a complete absence of clinically significant symptoms of depression, the optimal MADRS cutoff was ≤ 4. Based on a broader definition, the optimal cutoff was ≤ 9. Compared with patients scoring 5 through 9 on the MADRS, those who met the narrow definition of remission were rated higher, indicating better functioning, on the GAF, and reported significantly less psychosocial impairment.

Conclusion: Our results support the use of a low cutoff on the MADRS to define remission. Because the choice of cutoff will impact on the percentage of patients who are considered in remis-
There were few differences between the included patients and 289 whose symptom severity was too mild to qualify for an AET, characteristics of the 123 patients who would qualify for an AET, with the included patients the patients who would be excluded
tiveness of antidepressant efficacy trials (AETs) by applying typi-
ttempts, and were more likely to have a cluster B and cluster C
suicidal or had a comorbid anxiety or substance use disorder.
and the 187 patients who would be excluded because they were
due to comorbidity or suicidal ideation had more social impairment,
characteristics and psychosocial functioning of patients who would
clinical practice would not have qualified for an AET. In the present

tients, and found that most depressed patients treated in routine
clinical practice would not have qualified for an AET. In the present report we turn to the question of the comparability of the clinical characteristics and psychosocial functioning of patients who would and would not qualify for an AET.
Methods: 600 patients with a principal diagnosis of DSM-IV nonbipolar, nonpsychotic major depressive disorder (MDD) were interviewed by a trained diagnostic rater who administered the SCID and the Hamilton Depression Scale. The interview also included items from the SADS on social and occupational functioning. We determined the number of episodes, duration of the current episode, age of onset, and lifetime history of suicide attempts and hospitalizations. Nearly two-thirds (382) of the 599 depressed patients were interviewed with the SIDP for personality disorders.
Results: We compared demographic, psychosocial and clinical characteristics of the 123 patients who would qualify for an AET, 289 whose symptom severity was too mild to qualify for an AET, and the 187 patients who would be excluded because they were suicidal or had a comorbid anxiety or substance use disorder. There were few differences between the included patients and the excluded group due to low severity. In contrast, compared with the included patients the patients who would be excluded due to comorbidity or suicidal ideation had more social impairment, more frequently missed work because of psychiatric reasons, experienced more prior episodes, were more likely to have an epi-
sode duration of greater than two years, made more suicide at-
ttempts, and were more likely to have a cluster B and cluster C
personality disorder.
Conclusion: The findings of the present study raise additional caution in generalizing the results from AETs to clinical popula-
tions.

References:
1. Zimmerman M, Mattia JI, & Posternak M. (2002): Are subjects in pharmacological treatment trials of depression representa-

NR700  Wednesday, May 5, 3:00 p.m.-5:00 p.m.
Are There Differences Between Depressed Psychiatric Outpatients Who Would and Would Not Qualify for an Antidepressant Efficacy Trial?
Mark Zimmerman, M.D., Department of Psychiatry, Rhode Island Hospital, 235 Plain Street, Suite 501, Providence, RI 02905; Michael A. Posternak, M.D., Iwona Chelminski, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to describe differences between depressed psychiatric outpatients who would and would not qualify for an antidepressant efficacy trial.

Summary:
Background: Previously, our group examined the representa-
tiveness of antidepressant efficacy trials (AETs) by applying typi-
cally used exclusion criteria to a large sample of depressed outpa-
tients, and found that most depressed patients treated in routine clinical practice would not have qualified for an AET. In the present report we turn to the question of the comparability of the clinical characteristics and psychosocial functioning of patients who would and would not qualify for an AET.

Method: Two hundred and sixty-seven depressed outpatients were rated on the HRSD and completed the Clinically Useful Depression Outcome Scale (CUDOS). We used Receiver Operating Curve analysis to examine the sensitivity, specificity and overall classification rate of the CUDOS for identifying remission on the HRSD.

Results: In the ROC analysis the area under the curve was significant (AUC=.95, p<.001). The sensitivity, specificity and overall classification rate of the CUDOS for identifying remission according to the HRSD threshold of ≤7 was examined for each CUDOS total score. Several cutoffs were associated with similar overall levels of agreement, and changing the cutoff score to distinguish remitted and nonremitted patients resulted in the pre-
dictable corresponding changes in sensitivity and specificity, with increases in sensitivity accompanied a decrease in specificity. At the cutoff providing the best balance of sensitivity (87.4%) and specificity (87.8%), the total agreement level was 87.6%, and kappa was .75.

Conclusion: Self-report questionnaires represent a practical op-
tion for thoroughly and objectively evaluating the course of treat-
tment and determining remission status in depressed patients.

References:

NR702  Wednesday, May 5, 3:00 p.m.-5:00 p.m.
Is the HRSD Cut-Off to Define Remission Too High?
Mark Zimmerman, M.D., Department of Psychiatry, Rhode Island Hospital, 235 Plain Street, Suite 501, Providence, RI 02905; Michael A. Posternak, M.D., Iwona Chelminski, Ph.D.
**Educational Objectives:**

At the conclusion of this presentation, the participant should be able to describe approaches toward validating different cutoffs on the HRSD to define remission.

**Summary:**

*Background:* The Hamilton Rating Scale for Depression (HRSD) is the most frequently used measure of response in antidepressant efficacy trials (AETs). In characterizing treatment outcome in AETs, it is common to define remission as a score below a predetermined cutoff score on the scale. More than a decade ago a consensus panel published their recommendations that remission be defined on the 17-item version of the HRSD as a cutoff ≤7. This recommendation was accompanied by a call for research to validate this cutoff value. The goal of the present study was to examine the validity of this cutoff for defining remission.

*Methods:* Three hundred and three depressed psychiatric outpatients were rated on the Standardized Clinical Outcome Rating Scale for Depression, an index of DSM-IV remission status, the HRSD, and the Global Assessment of Functioning (GAF) scale. We examined the sensitivity, specificity, and overall classification rate of the HRSD for identifying a broad and narrow interpretation of the DSM-IV definition of remission, and the association between the breadth of the definition of remission, and self-report ratings of global psychosocial functioning and quality of life.

*Results:* Based on a narrow definition of remission, which requires an absence of clinically significant symptoms of depression, the optimal 17-item HRSD cutoff was ≤2. Compared with patients scoring 3 through 7 on the HRSD, those who scored 0-2 reported significantly less psychosocial impairment and better quality of life.

*Conclusion:* Our results support the use of a lower cutoff on the HRSD than has been traditionally been used to define remission. Because the choice of cutoff will impact on the percentage of patients who are considered in remission, and thus impact upon conclusions about treatment effectiveness, more empirical study should be directed towards this issue.

**References:**


**NR703 Wednesday, May 5, 3:00 p.m.-5:00 p.m.**

**Efficacy of Indiplon-MR in Inducing and Maintaining Sleep in Patients With Chronic Sleep Maintenance Insomnia**

*Supported by Neurocine Biosciences, Inc.*

Martin B. Scharf, Ph.D., Tristate Sleep Disorders Center, 1275 East Kemper Road, Cincinnati, OH 45264; Thomas Roth, Ph.D., James K. Walsh, Ph.D., Philip Jochelson, M.D., Melinda Garber, B.A.

**Educational Objectives:**

The research data presented will contribute to the participant’s understanding of the treatment of sleep maintenance insomnia with indiplon, a new investigational treatment for insomnia.

**Summary:**

*Objective:* The modified release formulation of indiplon, a novel GABA-A receptor potentiator, was evaluated for the treatment of sleep maintenance insomnia.

*Methods:* Adult outpatients (N=211; 68% female; mean age, 48 years) who met DSM-IV criteria for primary insomnia for ≥3 months, with usual subjectively-rated total sleep time (STST) <6.5-h, and wake after sleep onset (WASO) ≥45-mins, completed a two-week placebo lead-in, then were randomized to two weeks of double-blind, parallel-group nightly treatment with indiplon-MR 30mg vs. placebo. The primary endpoint was STST; secondary endpoints included latency to sleep onset (LSO), WASO, sleep quality and patient global impression (PGI) ratings.

*Results:* STST was significantly increased on indiplon-MR compared to placebo both at week 1 (375-mins vs. 328-mins; p<0.0001) and at week 2 (367-mins vs. 336-mins; p=0.0013). All secondary sleep maintenance measures also demonstrated significant improvement on indiplon-MR compared to placebo. Mean LSO was significantly improved on indiplon-MR both at week 1 (29.8-mins vs. 37.4-mins; p=0.0084) and at week 2 (27.3-mins vs. 33.2-mins; p=0.0131). WASO, sleep quality and PGI were significantly improved (p<0.005) on indiplon-MR at both weeks of treatment.

*Conclusions:* In patients with chronic primary insomnia, indiplon-MR 30 mg was well-tolerated and effective in inducing and maintaining sleep.

**References:**


**NR704 Wednesday, May 5, 3:00 p.m.-5:00 p.m.**

**Efficacy and Safety of Indiplon Immediate Release in Elderly Patients With Chronic Insomnia**

*Supported by Neurocine Biosciences, Inc.*

Martin B. Scharf, Ph.D., Tristate Sleep Disorders Center, 1275 East Kemper Road, Cincinnati, OH 45264; Russell Rosenberg, Ph.D., Martin Cohn, M.D., Gary K. Zammit, Ph.D., Philip Jochelson, M.D.

**Educational Objectives:**

The research presented in this poster will contribute to the participant’s understanding of the treatment of chronic insomnia in the elderly; and the safety and efficacy of indiplon, an investigational treatment for insomnia.

**Summary:**

*Objective:* The efficacy of immediate-release indiplon, a GABA-A potentiator, was evaluated by polysomnography (PSG) in elderly chronic insomnia patients.

*Methods:* Adults age 65–82 (N=42; 76% female; mean age, 70 years) who met DSM-IV criteria for primary insomnia for ≥3 months, and additional PSG criteria, were randomized, double-blind, to crossover treatment with three doses of indiplon-IR (5, 10, 20mg) vs. placebo. The primary PSG endpoints, based on a single night in the laboratory in each condition, included latency to persistent sleep (LPS) and total sleep time (TST). Subjective data were also collected. Next day effects were evaluated by the Digit Symbol Substitution Test (DSST) Symbol Copying Test (SCT) and a Visual Analog Scale of sleepiness (VAS).

*Results:* LPS was significantly reduced (p=0.001) for all indiplon doses relative to placebo (5mg: 13.8 min; 10mg: 10.4 min; 20mg: 9.8 min; placebo 25.2 min). TST was significantly increased on indiplon-10mg and -20mg, but not on the 5mg dose. Subjective rates of LSO, TST and sleep quality were similar vs. placebo for all three doses of indiplon. The DSST, SCT and VAS all showed no next-day difference for indiplon vs. placebo. Indiplon-IR was well-tolerated.
Conclusions: Indiplon-IR was effective in improving sleep onset and duration in elderly patients with chronic insomnia. It was well-tolerated with no significant next-day effects.

References:

NR705   Wednesday, May 5, 3:00 p.m.–5:00 p.m.
Post-Operative Sedation and the Incidence of Delirium in Cardiac Patients
Supported by Abbott Laboratories

Jose R. Maldonado, M.D., Department of Psychiatry, Stanford University, 401 Quarry Road, Room 2317, Stanford, CA 94305; Ashley Wysong, M.S., Thaddeus S. Block, M.D.

Educational Objectives:
At the conclusion of this session, participants should be able to understand the unique characteristics of the novel anesthetic, dexmedetomidine, and how it may help reduce the incidence of delirium in post-operative cardiac patients, and the broader implications of novel anesthetic use related to C/L psychiatry.

Summary:
Objectives: To determine if postoperative sedation is associated with the development of ICU delirium. Specifically, to understand the unique characteristics of dexmedetomidine and how it may reduce the incidence of postoperative delirium in cardiac surgery patients.

Methods: Ninety patients undergoing elective cardiac surgery were included in this prospective, randomized trial. All participants underwent a battery of neuropsychiatric tests prior to surgery and received similar general anesthesia consisting of a combination of inhalation agents, intravenous sedatives and opioids. Patients were randomly assigned to three post-operative sedation protocols: dexmedetomidine, propofol, or fentanyl/midazolam, started intraoperatively at sternal closure. Patients were followed for the development of delirium and neurocognitive deficits.

Results: Preliminary results of the first 60 patients show an incidence of delirium of 5% (1/21) for patients on dexmedetomidine, 52% (12/23) for propofol, and 50% (8/16) for midazolam. Additionally, dexmedetomidine patients spent less time in the ICU and had a shorter overall duration in the hospital when compared to the other two groups.

Conclusions: Postoperative sedation with dexmedetomidine may be associated with a lower incidence of post-operative delirium when compared with the use of more conventional forms of postoperative sedation. Although these findings are preliminary, several important trends exist that warrant further investigation.

Funding Source(s): Abbott Laboratories

References:

NR706   Wednesday, May 5, 3:00 p.m.–5:00 p.m.
Suicidality Reduction in Mixed Bipolar I Patients Receiving Olanzapine Co-Therapy
Supported by Eli Lilly and Company

John P. Houston, M.D., Department of Neuroscience, Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285; Christopher Kaiser, Ph.D., Elisabeth L. Degenhardt, M.S., Jonna Ahl, Ph.D., Hillary M. Easom, M.Ed., Robert W. Baker, M.D., Mauricio F. Tohen, M.D.

Educational Objectives:
At the conclusion of this session, participants should be able to understand some of the underlying clinical factors in suicidality in mixed bipolar I patients and how they may be affected by olanzapine cotherapy with valproate or lithium.

Summary:
Background: Correlation between suicidality reduction and psychiatric symptom improvement was assessed in patients with bipolar disorder, acute mixed mania, who were partially nonresponsive to >2 weeks of valproate or lithium monotherapy (MON) and subsequently treated with olanzapine (5-20mg/d) co-therapy (OLZ).

Methods: Post-hoc evaluations were correlation analysis between Hamilton Depression Rating Scale (HAM-D) Item 3 in patients with non-zero baseline scores (mean 1.44; N=57) and 67 items from Young Mania Rating Scale, HAMD-21, Positive and Negative Syndrome Scale, and Barnes Akathisia Scale, and factor analysis of items correlated at ≥0.20.

Results: Significant suicidality (HAM-D-3) reduction occurred by Week 1 with MON (Δ=-.84; N=22) vs. OLZ (Δ=-.04; N=36; p=0.42). Baseline factor analysis on HAMD-3 and 16 items correlated at ≥0.20 yielded 5 factors accounting for 66.2% of the variation. Factors corresponded to measures of clinical features associated with restlessness, psychosis, somatization, psychological depression, agitation. HAMD-3 loaded most heavily on somatization. Compared to MON patients, OLZ patients showed greater improvement (p<.05) in somatization by Week 1; restlessness, psychological depression, agitation by Week 2; psychosis by Week 3.

Conclusion: Mixed episode bipolar I patients treated with OLZ co-therapy after being non-responsive to MON experienced a rapid reduction in residual suicidality. Correlated suicidality-related factors were somatization, restlessness, psychosis, psychological depression, agitation.

Funding Source: Eli Lilly and Company

References:

NR707   Wednesday, May 5, 3:00 p.m.–5:00 p.m.
Suicidal Ideation Changes in Depressed Bipolar I Patients With Olanzapine-Fluoxetine Combination
Supported by Eli Lilly and Company

John P. Houston, M.D., Department of Neuroscience, Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285; Elisabeth L. Degenhardt, M.S., Jonna Ahl, Ph.D., Hillary M. Easom, M.Ed., Christopher Kaiser, Ph.D., Bruce J. Kinon, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to understand the clinical features that determine suicidality in depressed bipolar I patients and how they are treated with olanzapine.
Summary:

Objective: Correlation between non-zero baseline suicidal ideation (mean=2.21) and other clinical symptom severity measures was assessed post-hoc in olanzapine-fluoxetine combination (OFC), olanzapine (OLZ), and placebo-treated depressed patients with bipolar I disorder (N=688). Primary objective was determining the reduction in suicidality and associated measures by OFC (6–12/25–50mg/d) vs. OLZ (5–20mg/d).

Methods: Suicidal ideation was measured with Montgomery-Asberg Depression Rating Scale suicide item 10 (MADRS-10). Five of 21 Young Mania Rating Scale and MADRS items had a correlation coefficient >0.20 with MADRS-10: apparent sadness, reported sadness, inner tension, pessimism, suicidality (MADRS-1,2,3,9,10).

Results: Significant reduction in suicidality, measured by MADRS-10, occurred by Week 1 in patients receiving OFC (N=70) vs. OLZ (N=285;p=0.002) and placebo (N=298;p<0.001); by Week 3 in patients receiving OLZ (N=243) vs. placebo (N=259;p=0.020). Significantly greater improvement on all five items was achieved by Week 1 with OFC vs. placebo. OLZ patients showed significantly greater improvement vs. placebo in apparent and reported sadness at Week 1, inner tension and suicidal thoughts at Week 3, pessimism at Week 6.

Conclusion: Reduction in suicidal ideation in depressed bipolar I patients treated with OFC and OLZ was correlated with reducing dysphoria, pessimism, and inner tension.

Funding Source: Eli Lilly and Company

References:

Efficacy of Extended-Release Bupropion for the Prevention of Seasonal Depressive Episodes Supported by GlaxoSmithKline


Educational Objectives:
- At the conclusion of this session, the participant should recognize that once-daily treatment with extended-release bupropion is safe and well tolerated when used for the prevention of seasonal depressive episodes.

Summary:

Introduction: Bupropion is an effective antidepressant agent that is associated with low risk of sexual dysfunction, weight gain, or sedation.

Objective: To evaluate the safety and tolerability of bupropion XL used as a prophylactic treatment in patients with a history of Seasonal Affective Disorder.

Methods: Data from two identical studies were pooled. 614 subjects, who met DSM-IV criteria for Major Depressive Disorder with a seasonal pattern were randomized to receive 150–300 mg/day of bupropion XL or matching placebo. Bupropion was initiated in the fall, prior to the onset of a depressive episode, and continued to the first week of April. Clinical assessment of safety and tolerability occurred weekly for the first two weeks of treatment and biweekly thereafter.

Results: Bupropion XL was well tolerated with only 7.5% randomized patients discontinuing due to an adverse event. Side effects occurring in the bupropion XL group which were reported by more than 5% of patients and at a rate exceeding twice that observed with placebo were limited to constipation (9%), and tinnitus (6%). Rates of sexual dysfunction, weight gain, and sedation were comparable to placebo. No drug related serious adverse events occurred.

Conclusion: Bupropion XL treatment was well-tolerated when used for the prevention of seasonal depressive episodes.

Funding Source(s): GlaxoSmithKline

References:
2. Croft H, Settle Jr. E, Rouser T, Batey SR, Donahue RMJ, Ascher JA: A placebo-controlled comparison of the antidepress-

NR710 WITHDRAWN

NR711 Wednesday, May 5, 3:00 p.m.-5:00 p.m.
Modafinil for Major Depression With Atypical Features
Supported by Cephalon, Inc.
Kathryn M. Connor, M.D., Department of Psychiatry, Duke University, Box 3812 DUMC, Durham, NC 27710; Kishore M. Gadde, M.D., Wei Zhang, M.D., Victoria M. Payne, M.D., Jonathon R.T. Davidson, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to: (1) recognize the potential role of Modafinil in treating major depressive disorder with atypical features; and (2) describe the therapeutic effects of Modafinil in atypical depression.

Summary:
Objective: Augmentation with psychostimulants benefits some patients with treatment refractory depression, particularly those with significant fatigue and hypersomnia. The novel stimulant Modafinil has shown benefit as adjunctive therapy in anergic depression and is approved for excessive daytime sleepiness in narcolepsy, suggesting a potential role in atypical depression. This study examined modafinil as monotherapy in adult outpatients with major depression with atypical features.

Method: Subjects with atypical depression were treated with open-label Modafinil for 12 weeks. Efficacy assessments included measures of depression, fatigue and sleep. Safety evaluation included changes in vital signs and weight and emergence of adverse events.

Results: Preliminary analysis of subjects enrolled to date (n=37) revealed a study sample which was predominantly female (n=36), Caucasian (n=27), and unmarried (n=23), with a mean age 41 years. 30 subjects (81%) completed the treatment period. Results for all subjects enrolled in the open-label will be presented.

Conclusion: These findings suggest a role for the novel stimulant Modafinil in the treatment of major depression with atypical features.

Study sponsored by a grant from Cephalon, Inc to Dr. Davidson.

Funding Source(s): Psychiatrists, psychologists, other physicians and health care providers, researchers

References:

NR712 Wednesday, May 5, 3:00 p.m.-5:00 p.m.
Duloxetine Treatment of MDD: Safety and Efficacy Supported by Eli Lilly and Company
Madelaine M. Wohlreich, M.D., Department of Neuroscience, Eli Lilly & Company, 5202 Potters Pike, Indianapolis, IN 46234; Craig H. Mallickcrodt, Ph.D., John G. Watkin, D.Phil., Apurva Prakash, B.S.

Educational Objectives:
At the conclusion of this session, participant should recognize that duloxetine, a potent and balanced dual reuptake inhibitor of serotonin and norepinephrine, has demonstrated safety and tolerability at once-daily doses above 60 mg, and that rapid dose escalation can be achieved without incurring additional adverse events.

Summary:
Background: Duloxetine, a dual reuptake inhibitor of 5-HT/NE, has demonstrated efficacy for the treatment of major depressive disorder (MDD) in double-blind, placebo-controlled trials. While the expected starting and therapeutic dose is 60 mg QD, we further investigated duloxetine’s pharmacologic profile by examining its safety and tolerability during dose escalation from 60mg QD to 120mg QD.

Method: Patients with MDD (n=128) received: placebo one week then duloxetine 60mg QD one week, 90mg QD one week, and 120mg QD four weeks. Safety was assessed using spontaneously reported treatment-emergent adverse events (TEAEs), changes in vital signs, and laboratory analytes.

Results: The discontinuation rate due to TEAEs (16.3%) was comparable to rates observed in previous placebo-controlled trials. The most frequently reported TEAEs were nausea, headache, dry mouth, dizziness, and decreased appetite. The majority of TEAEs were associated with initial duloxetine dosing—dose escalations produced few additional TEAEs. Mean changes from baseline to endpoint in supine systolic and diastolic blood pressure were 1.2 and 0.6 mm Hg, respectively, with no reports of sustained hypertension.

Conclusion: These results establish the safety and tolerability of duloxetine at once-daily doses above 60 mg, and demonstrate that rapid dose escalation can be achieved without incurring additional adverse events.

Funding Source: Eli Lilly and Company

References:

NR713 Wednesday, May 5, 3:00 p.m.-5:00 p.m.
The Epworth Sleepiness Scale as a Screening Tool for Sleepiness in Depression
Supported by Cephalon, Inc.
Leslie Lundt, M.D., Foothills Psychiatry, 223 West State Street, Boise, ID 83702

Educational Objectives:
At the conclusion of this session, the participant should recognize the potential of effective baseline screening for sleepiness in psychiatric practice, which may help to define better treatment options and possibly prevent future depressive episodes.

Summary:
Objective: The Epworth Sleepiness Scale (ESS) is an easily patient-administered scale used by sleep specialists to estimate the extent to which sleepiness interferes with daily activities. This retrospective study evaluated the incidence of sleepiness using the ESS at initial visit in patients with depression and determined if there was a significant correlation between sleepiness severity and mood level.
Method: Consecutive patients seen in a psychiatric facility between February 2001–December 2002 with a current or previous diagnosis of major depressive disorder (single episode or recurrent) were included. Diagnoses were clinically conducted or confirmed using the Beck Depression Scale and interviews. Patients completed an ESS questionnaire during initial visit to determine sleepiness severity.

Results: 86 of 161 patients (55%) presented with an ESS total score of <10 (mean±SD=5.6±2.5) at initial visit; 73 patients (45%) with an ESS ≥10 (mean=13.5±3.0), indicating excessive sleepiness 92 (57%) patients were taking antidepressant medication. A correlation analysis of the ESS and Beck scale showed a significant causal relationship between sleepiness severity and depression level (p<.0001). The mean Beck Depression score for patients with an ESS total score of <10 versus ≥10 was 23.3±11.3 versus 30.1±11.5 (p=0.02), respectively.

Conclusion: Patients with depression commonly have sleepiness when presenting to their psychiatric facility. The ESS is an appropriate tool for assessing excessive sleepiness in clinical psychiatry.

References:

NR714 Tuesday, May 4, 12:00 p.m.–2:00 p.m.
MDD and Comorbid Chronic Pain: A Costly Condition Supported by Eli Lilly and Company

Enid M. Hunkeler, M.A., Research Division, Kaiser Permanente, 3505 Broadway, 7th Floor, Oakland, CA 94611; Bruce A. Amor, Ph.D., Janelle Lee, M.H.A., Christine Blasey, Ph.D., Bruce Fireman, M.S., Rebecca Robinson, M.S., Robin A. Dea, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should recognize that major depressive disorder and comorbid chronic disabling pain needs to be addressed in primary care.

Summary:
Depression is costly. Depression with comorbid chronic pain may cost more. We analyzed patterns of utilization and medical care costs among 5,908 respondents to a survey mailed to a random sample of adults following a visit to a primary care clinic at Kaiser Permanente in Northern California in 2002. We found 8.1% of respondents had major depressive disorder (MDD) (ascertained by the PHQ-8), 13% had disabling chronic pain (ascertained by the Graded Chronic Pain Scale), and 32% had chronic pain without disability. Utilization and costs during 2001 were compared by whether patients reported (1) neither depression nor pain (None), (2) non-disabling chronic pain only (P), (3) disabling chronic pain only (DP), (4) MDD only, (5) MDD+P, and (6) MDD+DP. In each group, respectively, average health care costs (±SE) were: $2,879(152), $3,325(198), $6410(351), $4145(696), $7,105(825), and $8,558(637). The 41% of MDD patients with MDD+DP were 2-3 times more costly than patients with MDD only (P=0.01) with respect to every cost category examined: hospital, clinic, pharmacy and total costs. It is important to address comorbid MDD and disabling chronic pain in primary care.

References:

NR715 Wednesday, May 5, 3:00 p.m.–5:00 p.m.
Cognitive Effects of Risperidone Augmentation In Treatment-Resistant Depression Supported by Janssen Pharmaceutica and Research Foundation

Carla M. Canuso, M.D., Janssen Pharmaceutica Products, L.P., 1125 Trenton-Harbourton Road, Titusville, NJ 08560; Gahan J. Pandina, Ph.D., Cynthia Bossie, Ph.D., Amy Loescher, B.S., Ibrahim Turkoz, M.S., Georges Gharabawi, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to discuss the cognitive effects associated with risperidone augmentation of SSRI monotherapy in patients with unipolar treatment-resistant depression.

Summary:
Background: Research suggests that risperidone has a rapid, robust effect on symptoms of treatment-resistant depression (TRD) and also improves cognitive function in patients with schizophrenia. This study was designed to assess cognition in patients with TRD who are participating in an ongoing trial of risperidone augmentation for TRD.

Methods: Patients with unipolar depression and at least one historical failure to an antidepressant were given SSRI (citalopram) monotherapy for 4–6 weeks. Those who failed to respond to citalopram were eligible to receive open-label risperidone augmentation for 4–6 weeks. Cognitive assessments of working memory, executive function, secondary memory, attention, and simple motor speed were carried out during the SSRI phase and after 4–6 weeks of risperidone augmentation. Cognitive function was assessed with Cogtest, a computerized neurocognitive test battery (Cogtest plc, London).

Results: A total of 267 patients completed at least one cognitive test. Compared with the end of the SSRI phase, risperidone augmentation resulted in statistically significant (P<0.05) improvements in tests of working memory, executive function, and attention in these treatment-resistant patients. Secondary memory and simple motor speed did not significantly change.

Conclusion: These data suggest that risperidone augmentation may improve cognition in patients with TRD. Further research is warranted.

Supported by Janssen Pharmaceutica Products, L.P.

References:

NR716 Wednesday, May 5, 3:00 p.m.–5:00 p.m.
Comparative Efficacy of Sertraline and Venlafaxine Extended Release in MDD Supported by Pfizer Inc.

Russell F. D’Souza, M.D., Continuing Care Psychiatry, Mental Health Research Institute, Level 1, 43 Carrington Road, Box...
**NR718** Wednesday, May 5, 3:00 p.m.-5:00 p.m.

**Efficacy of Mirtazapine Treatment of Major Depressive Episode due to Parkinson's Disease Supported by Organon Inc.**

Roberto L. Weiser, M.D., *Neurology Movement Disorders Unit, Hospital Universitario de Caracas, Apartado Postal 546, Caracas 1010, Venezuela; Julio Flores, Jorge Hernandez, M.D., Marisol Gallardo, M.D., Maria Garcia, M.D., Grau Miguel, M.D.*

**Educational Objectives:**

At the conclusion of this session, the participant should be able to discuss the efficacy of mirtazapine in the treatment of depressed patients with Parkinson disease.

**Summary:**

**Objective:** To assess efficacy, tolerability and safety of mirtazapine in depressed patients with Parkinson disease.

**References:**


**Funding Source(s):** Supported by Organon Venezolana SA.

**Methods:** Subjects with major depressive episode and Parkinson disease (MDD-PD) according to the DSM-IV and London Brain Bank criteria were assessed in a double blind randomized, placebo-controlled trial, receiving mirtazapine 30 mg/d during eight weeks. Assessments were performed at baseline, week 1, 2, 4, 6 and 8, using HAM-D-17 and UPDRS III. Response was considered reduction ≥50% in HAM-D-17 and Remission as a score ≤ 7 at the end point.

**Results:** ITT was conformed by 20 patients. At the end point, a higher reduction on HAM-D-17 and UPDRS III was shown in the mirtazapine group (statistical significance only for HAM-D-17). More patients were classified as responders and remitters in the mirtazapine group at the endpoint. No drop outs reported in any group; peripheral edema was the only adverse event reported by one patient of the mirtazapine group.

**Conclusions:** Mirtazapine is an effective and safe option for the treatment of patients with MDD-PD, specially for severe cases.

**References:**


**Funding Source(s):** Supported by Organon Venezolana SA.

**NR719** Wednesday, May 5, 3:00 p.m.-5:00 p.m.

**Duloxetine in the Treatment of MDD: A Comparison of Efficacy in Patients With and Without Melancholic Features Supported by Eli Lilly and Company**

Craig H. Mallinckrodt, Ph.D., *Department of Neuroscience, Eli Lilly and Company, Lilly Corporate Center, DC 2206, Indianapolis, IN 46285; John G. Watkin, D.Phil., ChaoFeng Liu, Ph.D., Madelaine M. Wohlerich, M.D., Joel Raskin, M.D.*

**Educational Objectives:**

At the conclusion of this session, the audience should understand the importance of, and difficulty in treating patients who have major depression with melancholic features.

**Summary:**

**Introduction:** Evaluating new antidepressant pharmacotherapies in patients within major depressive subtypes (e.g. atypical, melancholic) is important in understanding a drug’s overall utility. The present investigation compared duloxetine in the treatment of major depressive disorder (MDD) in patients with and without melancholic features.

**Methods:** Efficacy data were pooled from eight double-blind, placebo-controlled clinical trials. Patients meeting DSM-IV criteria for MDD received duloxetine (40-120 mg/d; melancholic, n=759; non-melancholic, n=379) or placebo (melancholic, n=519; non-melancholic, n=256) for up to nine weeks. Patients were identified at screening as having or not having melancholic features based on the MINI.

**Results:** In data from all eight trials, duloxetine’s advantage over placebo did not differ significantly between melancholic and non-melancholic patients, and was significantly superior to placebo within the melancholic and non-melancholic cohorts (p ≤ .001 for HAMD-17 total score, CGI severity (CGI-S), and PGI improvement (PGI-I). In the two trials that assessed duloxetine 60 mg once daily, duloxetine was significantly superior to placebo on the HAMD-17, CGI-S, PGI-I, 4 of 5 subscales of the HAMD, and on overall pain as measured by a visual analog scale (p < .01).

**Conclusion:** Duloxetine was effective in the treatment of MDD, both in patients with and without melancholic features.

**Funding Source(s):** Eli Lilly and Company.
References:

NR720 Wednesday, May 5, 3:00 p.m.-5:00 p.m.
Tolerability and Discontinuation Effects for Sertraline Versus Venlafaxine Extended Release in Depression Supported by Pfizer Inc.

Aytekir Sir, M.D., Psychiatry Department, Dicleuni Medical Facility, Diyarbakir 21280, Turkey, Russell F. D’Souza, M.D., Sukru Uguz, M.D., Tom George, M.B., Fiona G. Molfroy, B.S.C., Bill Lam, M.D.

Educational Objectives:

- At the conclusion of this presentation, the participant should have an increased knowledge of the comparative safety and tolerability of venlafaxine-XR and sertraline in the treatment of major depression, as well as an increased knowledge of how to taper patients off treatment.

Summary:

**Objective:** To compare the safety and tolerability of sertraline vs venlafaxine-XR, including structured assessment of discontinuation symptomatology, based on the Signs & Symptoms of Discontinuation Scale (SSDS).

**Method:** An international, 8-week, double-blind study of outpatients with DSM-IV major depressive disorder (MDD; N=161; 70% female, mean age, 37 yrs; baseline HAM-D, 23) were randomized to sertraline (50-150 mg/day; n=79) and venlafaxine-XR (75-225 mg/day; n=82). At the end of 8 weeks of double-blind treatment, subjects tapered off medication at a rate not exceeding 50 mg of sertraline and 75 mg of venlafaxine-XR every 4 days.

**Results:** Mean week-8 doses were 105-mg for sertraline and 161-mg for venlafaxine-XR. A greater proportion of patients discontinued from venlafaxine-XR compared with sertraline (28% vs. 17%, p=0.09). During tapering, patients on venlafaxine-XR experienced more discontinuation symptomatology, with a ≥10% higher incidence for the following SSDS events compared to sertraline: dizziness (44% vs. 33%), vivid dreams (42% vs. 26%), fatigue (39% vs. 22%) and vertigo (17% vs. 6%). Time to completion of drug tapering was similar between treatments.

**Conclusions:** Although sertraline and venlafaxine-XR were found to be well-tolerated in the acute treatment of MDD, clear differences in discontinuation effects were found between sertraline and venlafaxine-XR during treatment withdrawal.

**Funding Source(s):** Pfizer Inc.

References:

NR721 Wednesday, May 5, 3:00 p.m.-5:00 p.m.
Early Weight Gain as Predictor of Substantial Weight Gain in Patients With Bipolar Disorder Supported by Eli Lilly and Company

Ilya Lipkovich, Ph.D., Department of Neuroscience, Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285;
Jonna Ahl, Ph.D., Saeed Ahmed, M.D., Patrick Toalson, R.Ph., Thomas Hardy, M.D., Diane Haldane, M.S., Mauricio F. Tohen, M.D.

Educational Objectives:

- At the conclusion of this session, participant should be able to demonstrate that early weight gain in patients treated with olanzapine may predict substantial weight gain later.

Summary:

**Objective:** To examine early weight gain (EWG) during olanzapine (OLZ) treatment as a predictor of substantial weight gain (SWG) later in treatment.

**Methods:** Data were pooled from two double-blind, multicenter international studies in bipolar patients who met symptomatic remission criteria for an index manic, depressed or mixed episode (N=103). Patients received OLZ 5-20 mg daily. Endpoint for this analysis was 29 weeks. SWG was defined as gaining at least 10 kg at endpoint, EWG was determined as gaining at least 2.4 kg in the first three weeks.

**Results:** EWG of 2.4 kg optimized discrimination of patients with SWG. Among patients with SWG (n=24) 66.7% also had EWG (sensitivity), and 63.3% of patients without SWG (n=79) did not have EWG (specificity). Among those patients who did not have EWG (n=58), 86.2% did not have SWG. Addition of baseline characteristics (age, gender, baseline BMI, non-white race) modestly improved predictability. Results for other SWG cut-offs were qualitatively similar.

**Conclusions:** EWG during treatment with OLZ predicted SWG later. Patients with lesser EWG appeared much less likely to have SWG. Further research is necessary to explore the predictability of EWG for SWG with OLZ, and other medications, particularly in patients with symptomatic bipolar disorder.

**Funding Source(s):** Eli Lilly and Company.

References:

NR722 Wednesday, May 5, 3:00 p.m.-5:00 p.m.
Efficacy of Duloxetine Treatment: Analysis of Pooled Data From Six Placebo- and SSRI-Controlled Clinical Trials Supported by Eli Lilly and Company

Ralph W. Swindle, M.D., Outcomes Research Department, Eli Lilly and Company, Lilly Corporate Center, DC4025, Indianapolis, IN 46285; Craig H. Mallinckrodt, Ph.D., Jerrold F. Rosenbaum, M.D., Yili Lu, Ph.D., John G. Watkin, D.Phil., Michael J. Detke, M.D.

Educational Objectives:

At the conclusion of this session, participant should be aware that duloxetine exhibited superior efficacy to that of SSRI comparators in treating anxiety symptoms associated with depression, based upon mean changes in the HAM-D17 anxiety subscale.

Summary:

**Objective:** Pooled clinical trial data were utilized to compare the efficacy of duloxetine with that of SSRI comparators using the *a priori* specified primary efficacy outcome—mean change in HAM-D17 total score.

**Methods:** Data were pooled from six double-blind clinical trials. Patients meeting DSM-IV criteria for major depressive disorder

[271]
NR723 Wednesday, May 5, 3:00 p.m.-5:00 p.m.
Risperidone Monotherapy in Acute Bipolar Mania: A Nine-Week Extension Trial in the United States Supported by Janssen Pharma Products, LP

Robert M.A. Hirschfeld, M.D., Psychiatry & Behavioral Science, University of Texas Medical Branch, 301 University Boulevard 1.302RSH, Galveston, TX 77555-0188; Marielle Eerdekens, M.D., Suzanne M. Sutherland, M.D., Carla M. Canuso, M.D., Keith Karcher, M.S.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to describe the safety and antimanic efficacy of open-label risperidone monotherapy in patients previously randomized to three weeks of either double-blind placebo or risperidone monotherapy for bipolar I disorder.

Summary:
Purpose: To examine the safety and efficacy of risperidone monotherapy for bipolar I disorder.

Methods: A nine-week, U.S.-based, open-label extension study was conducted in patients previously randomized to three weeks of either double-blind placebo or risperidone monotherapy. Primary outcomes were mean changes from open-label baseline to endpoint in Young Mania Rating Scale (YMRS) total scores, Extrapyramidal Symptom Rating Scale (ESRS) total scores, and body weight.

Results: Of the 83 patients in the study, 38 had been previously randomized to double-blind placebo (PLA/RIS) and 45 to risperidone (RIS/RIS). The study was completed by 60% of patients. The mean medium dose (SD) of risperidone was 3.5 (1.4) mg/day. Mean YMRS scores (SD) significantly improved from 14.4 (7.5) to 6.5 (6.8) (P < 0.001) in PLA/RIS patients and from 10.3 (6.9) to 8.2 (8.1) (P = 0.038) in RIS/RIS patients. Mean ESRS scores were 1.0 (2.6) at baseline and 1.4 (3.0) at endpoint in PLA/RIS patients and 1.2 (2.3) and 1.1 (2.1) in RIS/RIS patients. Mean body weight changes at endpoint were +0.1 kg in PLA/RIS patients and +0.4 kg in RIS/RIS patients.

Conclusion: Risperidone was well tolerated and significantly improved acute bipolar mania symptoms in patients previously treated with double-blind placebo or risperidone.

References:

NR724 Wednesday, May 5, 3:00 p.m.-5:00 p.m.
Efficacy and Safety of Quetiapine Compared With Divalproex Sodium for Treatment of Acute Mania Supported by AstraZeneca Pharmaceuticals

David E. Fleck, Ph.D., Department of Psychiatry, University of Cincinnati Medical School, 231 Albert Sabin Way, Cincinnati, OH 45267-0559; Eduardo Dunayevich, M.D., Shannon E. Knepley, R.N., K. Sagar Kakani, B.S., Kimberly B. Corey, M.A., Stephen M. Strakowski, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to compare quetiapine and divalproex sodium in terms of safety and efficacy in the treatment of adults with bipolar mania.

Summary:
Objective: To compare increasing doses of quetiapine to divalproex sodium (valproic acid; VPA) in adults with mania associated with bipolar disorder.

Methods: Twenty patients hospitalized for a manic or mixed episode of bipolar I disorder with psychotich features were randomly assigned to receive increasing doses of quetiapine (n=11) or VPA (n=9).

Results: Quetiapine was increased from 150 mg on day 1 to > 400 mg by day 4. Mean final dosages were 656 mg/d for quetiapine and 1607 mg/d for VPA. Repeated measures analysis of variance (with last observations carried forward for 4 noncompleters) indicated significant and similar reductions in overall and manic symptoms in both groups. However, significant decreases in Clinical Global Impression depressive symptoms were seen only with quetiapine. Both treatments were well tolerated. The most common differential adverse events were tremor (33% divalproex sodium vs 0% quetiapine), headache (22% vs 9%), and sedation (0% vs 18%).

Conclusion: These preliminary data suggest that while quetiapine, increased from 150 mg/d to 400 mg/d over 4 days, is equally as efficacious and well tolerated as VPA for treating mania, it is more efficacious in reducing depressive symptoms.

 References:
NR725  Wednesday, May 5, 3:00 p.m.-5:00 p.m.
Comparison of Quetiapine Versus Lithium Treatment of Resistant Depression
Supported by AstraZeneca Pharmaceuticals
Jean P. Doree, M.D., Department of Psychiatry, Hospital P. Legardeur, 135 Bd Claude David, Repentigny, QC J6A 1N6, Canada; S. Valerie Tourjman, M.D., Stephane Kunicki, M.D., Joel Desrosiers, M.D., Claude Vanier, M.D., Robert Eile, M.D., Viviane A. Lew, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to: (1) compare the efficacy of quetiapine and lithium in treating patients with treatment resistant major depression; and (2) describe the benefits to patients with treatment resistant major depression of augmenting antidepressant treatments with quetiapine.

Summary:
Objective: The 30% to 50% of patients who do not respond to antidepressant treatment require alternative treatment. This pilot study investigates the effects of augmenting antidepressant treatments using quetiapine and lithium in patients with treatment-resistant major depression.

Methods: Subjects (18–64 years) with a HAM-D of ≥20 after four weeks of treatment at maximal antidepressant dose were evaluated at Weeks 1, 2, 4, 6, and 8 using rating scales (HAM-D, MADRS, UKU, SAS, Widdloche) that paralleled standard clinical practice. In this eight-week, single-blind study patients were randomized to receive either quetiapine (400–800 mg/day) or lithium (600 mg/day, first two weeks; 0.8–1.2 mEq/L thereafter). Data were analyzed by 2×2 factorial ANOVA.

Results: Preliminary results show that depression (HAM-D) of patients in both treatment groups (8 patients in each group) improved significantly (F 1,26 =44.70, p<0.001) but to a greater extent with quetiapine (F 1,26 =9.89, p<0.01). A greater number of patients responded to treatment (88% vs 50%) and were in remission (88% vs 38%) in the quetiapine group compared with the lithium group. Similar results were observed with MADRS. Final results will be presented (10 patients in each group).

Conclusion: This study suggests that quetiapine may be a valuable alternative in the treatment of resistant depression.

Funding Source(s): AstraZeneca.

References:

NR726  Wednesday, May 5, 3:00 p.m.-5:00 p.m.
Comparative Efficacy of Sertraline Versus Venlafaxine Extended Release in Severe Depression Supported by Pfizer Inc.
Tom George, M.B., Suite 6 Northwest Specialist Centre, 137A Flockton Street, Everton Park, QLD 4053, Australia; Sukru Uguz, M.D., Russell F. D’Souza, M.D., Aytekir Sir, M.D., Elizabeth Y. Malout, Ph.D., Tai Burt, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should have an increased knowledge of the management of the more severe forms of major depression.

Summary:
Objective: To compare antidepressant efficacy of sertraline versus venlafaxine-XR in a subgroup of depressed patients with severe depression.

Method: An international, 8-week, double-blind study of 161 outpatients with Major Depressive Disorder (MDD) who were randomized to sertraline (50–150 mg/day) and venlafaxine-XR (75–225 mg/day) followed by 2-week taper. A severe depression subgroup was defined by baseline HAM-D total score ≥26 or CGI-S ≥5. Response was defined as >50% reduction in HAM-D; remission was defined as HAM-D ≤7. Intention-to-treat analyses were performed on the last observation carried forward (LOCF).

Results: 82 (51%) of 161 outpatients met criteria for severe MDD (74% female; mean age 36 years; mean baseline HAM-D 26). In this severe MDD subgroup, mean change from baseline on HAM-D total score was similar for sertraline versus venlafaxine-XR at week 8/LOCF (−17.8±1.7 vs −15.4±1.6; p=0.24) and for week 8 completers (−20.1±1.5 vs −17.9±1.5; p=0.25). At week 8/LOCF, HAM-D responder rates (71±67%; p=0.55) and HAM-D remission rates (58±45%; p=0.28) were comparable for sertraline and venlafaxine-XR, respectively.

Conclusions: Sertraline and venlafaxine-XR were found to have similar antidepressant efficacy in severe MDD.

Funding Source(s): Pfizer Inc.

References:

NR727  WITHDRAWN
NR728  Wednesday, May 5, 3:00 p.m.-5:00 p.m.
Mania Remission Rates and Euthymia With Quetiapine Combination Therapy
Supported by AstraZeneca Pharmaceuticals
Norman Sussman, M.D., Department of Psychiatry, NYU School of Medicine, 150 East 55th Street, 27th Floor, New York, NY 10155, Jamie Mullen, M.D., Dennis E. Switzer, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to: (1) evaluate efficacy data for quetiapine using three different criteria for remission/euthymia; (2) use the analyses presented to inform clinical practice when using quetiapine and/or mood stabilizers for the management of bipolar disorder.

Summary:
Objective: Analyze rates of remission/euthymia in patients with bipolar mania receiving quetiapine and/or one other mood stabilizer.

Methods: A pooled analysis of two double-blind studies of patients hospitalized with bipolar I mania who received quetiapine (up to 800 mg/day) in combination with lithium (0.7–1.0 mEq/L) or divalproex (50–100 g/mL) for up to six weeks. Three different criteria of remission/euthymia were used to determine efficacy: (i) YMRS score of 12 or less; (ii) YMRS<12 plus a MADRS score of 10 or less; and (iii) YMRS<12 + MADRS<8.

Results: Day 21 remission rates (YMRS<12) were 48.7% (90/185) with quetiapine combination therapy versus 33.0% (61/185) with lithium or divalproex alone (P=0.003). Rates of euthymia...
Levetiracetam: Efficacy and Tolerability in a Psychiatric Clinic Population Supported by UCB Pharma

Derrell W. Ray, M.D., Behavioral Solution, 1575 Northside Drive NW, Building 200, 160, Atlanta, GA 30318; Nancy Choate, R.N.

Educational Objectives:

At the conclusion of this session, the participant should be able to identify levetiracetam as a potentially useful psychopharmacologic agent in the clinic setting.

Summary:

Objective: Examine the effectiveness and tolerability of levetiracetam (LEV) when used to treat patients with a variety of psychiatric disorders in outpatient setting.

Introduction: LEV is a broad-spectrum antiepileptic with novel mechanisms of action and desirable PK and safety profiles.

Methods: 100 charts randomly identified from LEV treated patients were systematically reviewed. Eighty-five charts were evaluable.

LEV Response Score (LRS) was based on clinical impression and patient report, on a five-point scale (0 = no response, 1 = poor response, 2 = fair response, 3 = good response, 4 = excellent response).

Overall mean LRS was 2.1. Subjects with primary diagnoses of panic attacks, generalized anxiety disorder, or attention deficit hyperactivity disorder had better mean LRS than those who had major depressive disorder or bipolar disorder with less robustly (respectively, 1.96, 1.44). Forty-six out of 85 subjects (72%) reported no adverse events. Sedation and drowsiness were most commonly reported AE’s (n=9). Mean treatment duration was 6.7 months (range two weeks to 15.5 months). Seventy-two percent of subjects (61/85) remain on LEV. Average daily dose was 1540 mg/day (range 250-3000 mg).

Conclusion: LEV offers clinically relevant therapeutic benefit in a variety of psychiatric diagnoses. LEV is very well tolerated in the outpatient psychiatric clinical setting.

Funding Source(s): AstraZeneca, Wilmington, Delaware, USA

References:


NR730 Wednesday, May 5, 3:00 p.m.-5:00 p.m.

Olanzapine Treatment in Civilian PTSD With Comorbid Alcohol Dependence: An Open Study

Simon S. Chiu, M.D., Addiction Rehabilitation Unit, Regional Mental Health Care, St. Thomas Site, 467 Sunset Drive, St. Thomas, ON NSP 3V8, Canada

Educational Objectives:

At the conclusion of this session, the participant should be able to: (1) delineate the inter-relationships of childhood trauma, substance use, and PTSD; (2) and to evaluate critically the potential therapeutic efficacy of atypical antipsychotics in PTSD and comorbid substance abuse disorder.

Summary:

Introduction: With the high rates of substance use disorders in combat-related and civilian Post-Traumatic Stress Disorder (PTSD), the issue arises as to whether co-occurring substance abuse differentially modulates the therapeutic responses toward atypical antipsychotic agents in PTSD.

Objective: To evaluate the efficacy and tolerability of olanzapine in civilian PTSD with alcohol use co-morbidity and to examine whether olanzapine reduces episodes of alcohol relapse.

Methods: The design was open-label, naturalistic and prospective. Eighteen subjects (male/female: 9: 9) diagnosed as DSM-IV PTSD and co-occurring alcohol dependence entered into the study after four weeks of detoxification from alcohol. Flexible dosage of olanzapine was used for the 12-week period. Efficacy measures consisted of monthly assessments with Clinician Administered PTSD Scale (CAP-S), HAM-D (Hamilton Rating Scale for Depression), HAM-A (Hamilton Rating Scale for Anxiety), CGI I (Clinical global Impression-Improvement) score and self-report measures of alcohol use (Time line follow-back method) and Tiffany Craving questionnaire. Tolerability was monitored with the treatment emergent adverse events.

Results: Among the PTSD subjects, childhood trauma (sexual and physical abuse) preceded the onset of alcohol dependence and PTSD symptoms. Olanzapine was well tolerated at the average daily dosage of 15 mg (range 10-30 mg). As compared with baseline values, statistically significant reduction in PTSD symptoms (intrusive, hyperarousal and avoidance), HAM-D and HAM-A and improvement in CGI score were found during the 12-week treatment period (ANOVA, p < 0.01). While two subjects dropped out from the study, treatment completers reported significant reduction in alcohol consumption and Tiffany craving score (p< 0.05). Major side effects reported were increased appetite, weight gain, and restlessness.

Conclusion: The promising results in the pilot study suggest that olanzapine is useful and safe in PTSD with alcohol abuse co-morbidity, and merit randomized control trials to validate the efficacy of olanzapine in relapse prevention of PTSD and comorbid substance use disorder.

Funding Source(s): NIL

References:


Collins, Ph.D., Shawkat Hassan, M.S., Gregory de Lissovoy, Ph.D.

Educational Objectives:
After reading this poster, the participant will have an understanding of the strengths and limitations of administrative databases to study treatment patterns and outcomes of pharmacologic therapy, as demonstrated by a comparison of drugs commonly used to treat bipolar disorder.

Summary:
Objective: Compare resource use and costs among persons with bipolar disorder treated with delayed-release divalproex sodium (DVPX-DR), extended-release divalproex sodium (DVPX-ER), olanzapine (OLZ), and other atypical antipsychotics (risperidone and quetiapine (AA)) as single drug regimen or combination with lithium or other mood stabilizers (carbamazepine, gabapentin, lamotrigine, topiramate).

Methods: From a 2001–2002 managed care database we identified 9,733 persons age 18–64 with bipolar disorder and pharmacologic treatment. Episodes of continuous drug treatment were categorized by listed drugs (single drug or combinations). Resource use and costs were tabulated by episode.

Results: Duration of the first single or combination drug episode following 90 days free of study drug was longer for DVPX-ER (mean 94.9 days) than for DVPX-DR (82.4 days, p = 0.067), OLZ (70.0 days, p = 0.002), or AA (70.3 days, p = 0.002). Among single drug regimens, total cost of treatment including drug per patient-year of exposure to drug regimen was lower for DVPX-DR ($4436) than for DVPX-ER ($4887, p = 0.094), than OLZ ($6479, p = 0.002) or than AA ($7032, p = 0.006).

Conclusions: Persistence and treatment costs varied by drug treatment regimen. DVPX-DR and DVPX-ER were associated with longer duration of therapy and lower costs than OLZ or AA for single and combination episodes of listed drugs.

Funding Source(s): Abbott Laboratories

References:

NR732 Wednesday, May 5, 3:00 p.m.–5:00 p.m.
Hospitalization Rates With Atypical Antipsychotics in Bipolar Disorder
Supported by AstraZeneca Pharmaceuticals
Arthur L. Lazarus, M.D., Clinical Research Department, AstraZeneca L.P., 1800 Concord Pike, B3, Wilmington, DE 19850-5437; Maureen Lage, Ph.D., Jacqueline Pesa, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize lamotrigine as a pharmacologic alternative when treating adolescents diagnosed with Bipolar I Disorder.

Summary:
Objective: To evaluate the safety and efficacy of lamotrigine in the treatment of adolescent Bipolar I disorder (BD I), most recent episode depressed or mixed state.

Method: This was a single-center, outpatient, 12-week, open-label study in adolescents (ages 13–17) diagnosed with BD I, depressed or mixed. Twenty-three patients entered the trial and 13 completed 12 weeks of therapy. Children’s Depression Scale-Revised (CDRS-R), Young Mania Rating Scale (YMRS), Clinical Global Impression-Severity (CGI-S) were outcome measures.

Results: Baseline mean scores were: CGI-S = 4, CDRS-R = 73, and YMRS = 20 and at 12 weeks, scores were 1, 40, and 6, respectively. Mean starting dose of lamotrigine was 25 mg a day and at week twelve mean dose was 241 mg daily. Three subjects terminated early due to non-compliance, five were lost to follow-up, and two discontinued for suicidal ideation requiring hospitalization. No subjects discontinued for adverse events related to the study drug.

Conclusions: Lamotrigine appeared to be safe and efficacious in this population. Controlled studies are necessary to further evaluate the safety and efficacy of lamotrigine in this population.

Funding provided by GlaxoSmithKline
References:


NR734 Wednesday, May 5, 3:00 p.m.-5:00 p.m.
Clinical Features Associated With Maintenance Response in Bipolar I Disorder
Supported by Abbott Laboratories

James C.Y. Chou, M.D., Department of Psychiatry, New York University, 462 First Avenue, Room 20 West - 13, New York, NY 10016; Michelle Collins, Ph.D., Patricia J. Wozniak, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to evaluate the clinical features that are associated with a differential response to maintenance treatment in Bipolar I disorder.

Summary:

Recent maintenance trials in bipolar disorder have demonstrated the efficacy of divalproex, lamotrigine, olanzapine, and lithium. This report examines the predictive value of baseline clinical features in the large-scale divalproex trial (Bowden et al, 2000) that randomized 372 recently manic bipolar I patients to prophylactic treatment with divalproex, lithium, or placebo. Females had more relapses into depression than males, regardless of treatment, but divalproex's efficacy in females was greater in preventing mania. Both divalproex and placebo were superior to lithium in preventing depression in patients that were older at either their first bipolar episode or at time of study entry, and in non-psychotic patients (all p < 0.05). Divalproex was superior to lithium, but not placebo in preventing relapse to mania in patients whose first episode was mania, and in patients with fewer episodes per year (all p < 0.05). These results suggest differences in directional efficacy between divalproex and lithium. Gender, illness severity, age, and directionality of mood history predicted drug response. Lithium may be inferior for preventing depression in some patients, and there are mild patients who will do well on placebo.

Funding Source(s): Supported by Abbott Laboratories.

References:


NR735 Wednesday, May 5, 3:00 p.m.-5:00 p.m.
A Pilot Study Evaluating Osteoporosis in Women With Bipolar Disorder

Claudia F. Baldassano, M.D., Department of Outpatient Psychiatry, University of Pennsylvania, 3535 Market Street, 2nd Floor, Philadelphia, PA 19104-3309; Laszlo Gyulai, M.D., Emily Eisenstein, B.A.

Educational Objectives:

At the conclusion of this session, the participant should be able to understand whether women with bipolar disorder who take antiepileptic medication are at risk for the development of osteoporosis.

Summary:

Objective: Evaluate the effect of quetiapine on depressive symptoms in patients from double-blind studies of bipolar mania.

Methods: Depressive symptoms were assessed using the Montgomery-Asberg Depression Rating Scale (MADRS) in patients with bipolar I disorder (manic episode, DSM IV) who received quetiapine alone (up to 800 mg/day; 12 weeks) or combined with lithium (0.7–1.0 mEq/L) or divalproex (50–100 μg/mL) (3 or 6 weeks). Treatment-emergent depression, defined a priori as a MADRS score >/=18, with an increase from baseline of >/=4 at
any two consecutive assessments or at the last observation, was also monitored.

Results: In a combined analysis, the proportion of patients with treatment-emergent depression was low and similar in two monotherapy (quetiapine 4.3%, placebo 8.6%) and two combination therapy (quetiapine 10.7%, placebo 9.8%) studies. MADRS scores were reduced significantly with quetiapine monotherapy versus placebo at Day 21 (–2.44 vs. –0.78; P<0.001) and further at Day 94 (–5.61 vs. 0.06; P<0.001). No significant difference was observed between groups in change from baseline in MADRS scores with combination therapy.

Conclusions: Quetiapine as monotherapy and in combination with lithium/divalproex is not associated with emergent depression. Quetiapine treatment may improve depressive symptoms in patients with bipolar disorder.

Funding Source(s): AstraZeneca, Wilmington, Delaware, USA

References:

NR737 Wednesday, May 5, 3:00 p.m.-5:00 p.m.
Efficacy of Carbamazepine Extended Release for Adult Bipolar Patients
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 to discuss the effectiveness and safety of extended-release carbamazepine in the treatment of patients with bipolar disorder.

Summary:
Objective: To assess the effectiveness and safety of extended-release carbamazepine capsules (ERC-CBZ; SPD417) in the treatment of bipolar disorder.

Method: A chart review of 101 adult outpatients with DSM-IV bipolar disorder and treated with ERC-CBZ was conducted (mean age 32.8 ± 10.5 years; 71% female; 70% bipolar I, 18% bipolar II, 12% bipolar NOS). Charts of subjects who received ERC-CBZ in a private practice setting (LDG, Red Oak Psychiatry Associates, Houston, TX) between October 1998 and August 2003 were reviewed. Treatment response was assessed with the Clinical Global Impressions-Improvement (CGI-I) scale (1 = very marked improvement; 2 = moderate improvement). Relapse was defined as a mood change that occurs four weeks after initiation of medication or the return of symptoms from the original episode.

Results: Forty-four subjects (44%) taking ERC-CBZ had marked to moderate improvement (CGI-I score: 1.23%: 2, 21%). No subjects experienced moderate to marked worsening. Twenty-six patients (26%) relapsed during ERC-CBZ treatment (mean time to relapse = 180 days). Mixed symptoms were the most common bipolar illness presentation. The mean ERC-CBZ dose was 666.1 ± 267.8 mg/day and the mean serum concentration was 7.4 ± 2.3 µg/ml. Somnolence (9%) and nausea (8%) were the most frequently reported side effects.

Conclusion: Extended-release carbamazepine appears effective in the treatment of bipolar disorder and was well tolerated.

References:

NR738 Wednesday, May 5, 3:00 p.m.-5:00 p.m.
Quetiapine in Long-Term Adjunctive Treatment in Refractory Bipolar I Disorder
Mauro G. Carta, M.D., Department of Public Health, University of Cagliari, Via Liguera 13, Cagliari-Sardagna 09197, Italy; Maria C. Hardoy, M.D., Alessandra Garofalo, M.D., Bernardo Carpienr, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to consider the potential use of add-on quetiapine for the treatment of refractory bipolar I patients. This clinical option may be interesting because the degree of treatment resistance in bipolar patients is very high as suggested by recent findings.

Summary:
Objective: To determine the long-term effectiveness of adjunctive quetiapine for the relapse prevention in refractory bipolar I disorder.

Method: Twenty-one bipolar I outpatients inadequately responsive to standard treatments were treated in an open-label with adjunctive quetiapine (increasing doses until clinical response, 518±244 mg/day) for 26–78 weeks (n=13 >52 weeks). Illness response was assessed using the Clinical Global Impression Scale (CGI). Rates of relapses were compared before and during quetiapine treatment. Contrasts of rates of relapses between treatment phases were made by computing incidence risk ratios.

Results: Findings indicated highly significant differences in overall relapse rates between before versus during quetiapine treatment (12 ± 1.5person-years=0.5, risk ratio=2.9, CL95%, 1.5–5.6), in relapse rates into a manic/mixed episode between before versus during quetiapine treatment (8 ± 1.5person-years=0.98 vs. 6 ± 1.5person-years=0.3, risk ratio=3.3, CL95%, 1.5–7.1), and in relapse rates into a depressive episode between before versus during quetiapine treatment (4 ± 0.49 vs. 4 ± 0.5person-years=0.2, risk ratio=2.4, CL95%, 1.3–4.4). CGI mean scores showed a significant improvement during quetiapine treatment (n=21, baseline=4.57±0.98, week-12=3.81±0.75, week-26=3.67±0.80, F=6.92, P=0.002) and remained significant for improvement over a 52-week maintenance period (n=13, baseline=4.69±0.95, week-52=3.77±1.17, F=4.91, P=0.036).

Conclusions: Long-term treatment with adjunctive quetiapine reduced the probability of manic/mixed/depressive relapses in refractory outpatients with bipolar I disorder. Double-blind studies are needed to further confirm these results.

References:

NR739 Wednesday, May 5, 3:00 p.m.-5:00 p.m.
Antidepressant Switching Strategy for SSRI/SNRI Intolerance
Supported by GlaxoSmithKline
Lee D. Ruggiero, B.S., Glaxo Smith Kline, 2301 Renaissance Blvd., King of Prussia, PA 19406; Matini lyengar, M.D., Desiree Schafer, B.A., Alan Lipschitz, M.D.
**Educational Objectives:**

At the conclusion of this presentation, the participant will be able to evaluate the tolerability profile of paroxetine CR in treating depressed outpatients who could not tolerate a previous SSRI or SNRI regimen.

**Summary:**

*Objective:* To evaluate the safety and tolerability of controlled-release (CR) paroxetine in patients who stopped treatment with another SSRI or SNRI due to intolerance. To assess the adverse events (AEs) which caused intolerance of prior antidepressant and paroxetine CR treatment (recurrence).

*Methods:* Outpatients diagnosed with major depressive disorder who were intolerant and had stopped treatment with a recent (within two months) SSRI or SNRI regimen were treated with open-label paroxetine CR (flexible-dose, 12.5–62.5mg/day). The primary endpoint in this six-week study measured the proportion of patients withdrawing from the study due to a treatment emergent AE. Secondary endpoints measured the recurrence of AEs, overall AE incidence rates and summary statistics for efficacy data.

*Results:* The intent-to-treat population consisted of 646 patients. In total, 5.4% (35/646; 95% CI [3.6, 7.2]) of patients withdrew from the study due to a treatment emergent AE, 0.6% (4/646) withdrew due to lack of efficacy, and 86.2% (557/646) completed the six-week study. After switching to paroxetine CR, 12 (1.9%; 95% CI [0.7, 3.0]) patients withdrew due to AE and reported recurrent AEs which also caused intolerance to prior antidepressant. For example, nausea was reported by 15.3% (99/646) of patients as an AE causing intolerance of prior antidepressant. Only 3% (3/99) of these patients withdrew from the study due to nausea.

*Conclusion:* Switching patients previously intolerant to an SNRI or SSRI to paroxetine CR is a viable strategy for maintaining these patients on antidepressant treatment.

*Funding Source(s):* This study was funded by GlaxoSmithKline.

*References:*

**NR741 Wednesday, May 5, 3:00 p.m.-5:00 p.m.**

**The Long-Term Impact of Mood Stabilizers on Body Weight**

**Supported by GlaxoSmithKline**

Gary S. Sachs, M.D., Department of Psychiatry, Harvard-Massachusetts General Hospital, 15 Parkman Street WACC 815, Boston, MA 02114; Charles H. Merideth, M.D., Lawrence D. Ginsberg, M.D., Alan C. Swann, M.D., Thomas R. Thompson, M.D., Robin White, M.S., Connie Powers, B.S.

**Educational Objectives:**

At the conclusion of this session, the participant should be able to describe the impact of mood stabilizers on body weight in patients with bipolar I disorder in a long-term, placebo-controlled, randomized clinical study.

**Summary:**

*Introduction:* Despite the availability of effective treatments for bipolar disorder tolerability issues persist. Medication-related weight changes can negatively impact patient compliance with treatment.

*Objective:* To assess the long-term effect of lamotrigine on weight in patients with bipolar I disorder.

*Methods:* Weight data from 588 patients with bipolar I disorder in two long-term maintenance studies of lamotrigine (N=230), lithium (N=167), and placebo (N=191) were assessed. Analyses included observed mean weight change, proportion of patients with ≥7% change in weight and weight-related adverse events (AEs), and a mixed model repeated measures analysis of weight change over time.

*Results:* Observed mean weight changes were negligible and were similar for subjects receiving lamotrigine and placebo; mean weight for patients on lithium increased over time. The proportion of subjects experiencing clinically important (7%) weight changes and weight-related AEs were low and similar between the lamotrigine and placebo treatment groups. A mixed model repeated measures analysis showed that after one year of treatment, patients receiving lamotrigine and placebo had minimal mean weight changes (−1.2kg and +0.2kg, respectively) while patients receiving lithium experienced moderate weight gain (+2.2kg).

**NR740 Wednesday, May 5, 3:00 p.m.-5:00 p.m.**

**Reproductive Endocrine Function in Women Treated for Bipolar Disorder**

**Supported by Abbott Laboratories**

Lori L. Altshuler, M.D., Department of Psychiatry, University of California at Los Angeles, 300 Medical Plaza, Suite 1544, Los Angeles, CA 90024; Natalie L. Rasgon, M.D., Mohammad Saad, M.D., Shanah Elman, B.A., Willem A. Nolen, M.D., Jose A. Bitran, M.D., Mark A. Frye, M.D.

**Educational Objectives:**

At the conclusion of this session, participants should be able to understand the different endocrinologic effects of different antimanic agents; recognize the high rate of hormonal abnormalities in subjects with bipolar disorder that antedate treatment; recognize hyperandrogenemia as a marker of PCOS.

**Summary:**

*Objective:* This study sought to evaluate serum hormone levels in women with bipolar disorder; evaluating whether profiles differed as a function of antimanic medication.

*Method:* Bipolar women ages 18-45 who were not taking oral contraceptives were recruited to fill out questionnaires about their menstrual cycle and give blood samples to be measured for a range of reproductive endocrine and metabolic hormone levels. Seventy two women participated in the study.

*Results:* Several hormone levels were low (estrone and DHEAS) and others were high (HOMA and LH:FSH ratios) across the entire bipolar group. A significantly higher proportion of women taking DVPX had abnormal LH:FSH ratio values compared to those not taking DVPX. No other lab value was significantly associated with women as a function of their current medication. Mean levels of free and total testosterone, as well as the proportion of women with testosterone values outside the normal range were not significantly different in women taking vs not taking DVPX.

*Conclusions:* Many women with bipolar disorder had endocrine abnormalities, regardless of drug, that may contribute to high rates of menstrual disturbance reported in this population. High testosterone levels, a marker for PCOS, were not significantly different on or not on DVPX.

**References:**

**Conclusions:**

To evaluate the safety and tolerability of controlled-release (CR) paroxetine in patients who stopped treatment with another SSRI or SNRI due to intolerance. To assess the adverse events (AEs) which caused intolerance of prior antidepressant and paroxetine CR treatment (recurrence).

*Methods:* Outpatients diagnosed with major depressive disorder who were intolerant and had stopped treatment with a recent (within two months) SSRI or SNRI regimen were treated with open-label paroxetine CR (flexible-dose, 12.5–62.5mg/day). The primary endpoint in this six-week study measured the proportion of patients withdrawing from the study due to a treatment emergent AE. Secondary endpoints measured the recurrence of AEs, overall AE incidence rates and summary statistics for efficacy data.

*Results:* The intent-to-treat population consisted of 646 patients. In total, 5.4% (35/646; 95% CI [3.6, 7.2]) of patients withdrew from the study due to a treatment emergent AE, 0.6% (4/646) withdrew due to lack of efficacy, and 86.2% (557/646) completed the six-week study. After switching to paroxetine CR, 12 (1.9%; 95% CI [0.7, 3.0]) patients withdrew due to AE and reported recurrent AEs which also caused intolerance to prior antidepressant. For example, nausea was reported by 15.3% (99/646) of patients as an AE causing intolerance of prior antidepressant. Only 3% (3/99) of these patients withdrew from the study due to nausea.

*Conclusion:* Switching patients previously intolerant to an SNRI or SSRI to paroxetine CR is a viable strategy for maintaining these patients on antidepressant treatment.

*Funding Source(s):* This study was funded by GlaxoSmithKline.

*References:*
Conclusions: Long-term treatment with lamotrigine was not associated with clinically relevant changes in weight in patients with bipolar I disorder.

Funding Source(s): Research funded by GlaxoSmithKline

References:


NR742 Wednesday, May 5, 3:00 p.m.-5:00 p.m.
Aripiprazole Versus Placebo in Patients With an Acute Manic or Mixed Episode
Supported by Bristol-Meyers-Squibb and Otsuka Pharmaceutical Co., Ltd

Gary S. Sachs, M.D., Department of Psychiatry, Harvard-Massachusetts General Hospital, 15 Parkman Street WACC 815, Boston, MA 02114; Raymond Sanchez, M.D., Ronald N. Marcus, M.D., Mary J. Kujawa, M.D., Donald G. Archibald, Ph.D., William H. Carson, Jr., M.D., Taro Iwamoto, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to understand the efficacy and safety of aripiprazole for the treatment of acute manic or mixed episodes in patients with Bipolar I disorder.

Summary:

Objective: To compare the efficacy and safety of aripiprazole with placebo in patients with Bipolar I disorder experiencing an acute manic or mixed episode.

Methods: This Phase III, multicenter, double-blind, placebo-controlled study randomized 272 acutely manic patients with Bipolar I disorder to aripiprazole 30 mg/day (option to reduce to 15 mg for tolerability) or placebo for three weeks. Key outcome measures included the Young Mania Rating Scale (Y-MRS) Total Score, CGI-BP, and PANSS Hostility subscale.

Results: Aripiprazole produced significant improvements in the Y-MRS by day 4 and at endpoint compared with placebo (−12.5 vs −7.2, p ≤ 0.01). In addition, significantly more patients responded (Y-MRS decrease ≥50%) to aripiprazole vs placebo (53% vs 32%, p ≤ 0.01). Aripiprazole also showed significant improvement vs placebo on the CGI-BP Severity of Illness (mania) score and the PANSS Hostility subscale score. Aripiprazole and placebo had similar discontinuation rates due to AEs, while aripiprazole had fewer discontinuations due to lack of efficacy than did placebo. There were no significant changes in body weight vs placebo.

Conclusion: This is the second study to demonstrate the efficacy and safety of aripiprazole in the treatment of acute mania in patients with Bipolar I disorder.

Funding Source(s): Bristol-Myers Squibb Company and Otsuka Pharmaceutical Co., Ltd

References:


NR743 Wednesday, May 5, 3:00 p.m.-5:00 p.m.
Antianxiety Effects Analysis of Quetiapine in Bipolar Depression
Supported by AstraZeneca Pharmaceuticals

Wayne Macfadden, M.D., CNS Therapeutics, AstraZeneca, 1800 Concord Pike, PO Box 15437, Wilmington, DE 19850-5437; Joseph R. Calabrese, M.D., Robin McCoy, Margaret Minkwitz, Ellis Wilson, Jamie Mullen, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to: (1) recognize the benefit of quetiapine treatment for symptoms of anxiety in bipolar depression; and (2) understand that quetiapine may improve a broad range of symptoms when used to treat patients with bipolar disorder.

Summary:

Objective: Evaluate efficacy and safety of quetiapine monotherapy for anxiety symptoms in patients with bipolar depression.

Method: 511 patients (342 bipolar I, 169 bipolar II depression) who received eight weeks double-blind treatment with quetiapine (300 or 600 mg/d) or placebo were included in the efficacy analysis. Anxiety symptoms were assessed using the Hamilton Rating Scale for Anxiety (HAM-A).

Results: Mean baseline levels of anxiety measured by HAM-A score were similar across treatment groups: 18.6–18.9. Patients taking quetiapine 300 and 600 mg/d had significantly (P<0.05) greater improvement in mean HAM-A score vs placebo at every assessment starting with the first evaluation (Day 8) and sustained throughout endpoint (Week 8) (−8.6 and −8.7 vs −5.5). Common quetiapine adverse events (≥10% and ≥2x placebo rate) were dry mouth (43%), sedation (31%), somnolence (26%), dizziness (20%), and constipation (11%).

Conclusions: Quetiapine monotherapy (300 or 600 mg/d) is significantly more effective than placebo and well tolerated for the treatment of anxiety symptoms in patients with bipolar depression.

Funding Source(s): AstraZeneca, Wilmington, Delaware, USA

References:


pressant; continuation treatment with escitalopram has been shown to prevent relapse of a depressive episode.

**Methods:** Patients with recurrent major depression (at least two previous episodes; baseline MADRS >22) who have responded (MADRS score of 12 or less) to SSRI treatment in a lead-in trial received 16 weeks of flexible dose open-label escitalopram (10–20 mg/day) treatment. At the end of the lead-in phase, patients with MADRS <12 were randomized to 52 weeks of fixed dose double-blind treatment with escitalopram (10 or 20 mg/day) or placebo. Recurrence was defined as MADRS >= 22 or insufficient therapeutic response during the double-blind phase.

**Results:** A total of 203 patients received at least one dose of double-blind phase treatment. Cumulative recurrence rates were 30% for the escitalopram group and 62% for the placebo group (hazard ratio = 0.30; p<0.001). Crude recurrence rates were 26% for the escitalopram group and 53% for the placebo group (p<0.001). Long-term escitalopram treatment was well tolerated, with rates of discontinuation due to adverse events of 3.9%.

**Conclusion:** Maintenance treatment with escitalopram is well tolerated and significantly reduces the risk for recurrence of depressive episodes.

**Funding Source(s):** Forest Laboratories, Inc.

**References:**

**NR745**
**Wednesday, May 5, 3:00 p.m.-5:00 p.m.**
**Ziprasidone’s Long-Term Efficacy and Safety in Bipolar Disorder**

Paul E. Keck, Jr., M.D., Biological Psychiatry Department, University of Cincinnati, Medicine, 231 Albert Sabin Way, ML559, Cincinnati, OH 45267-0559; Steven G. Potkin, M.D., Earl Giller, Jr., M.D., Kathleen Ice, Ph.D., Lewis Warrington, Ph.D., Judith Dunn, Ph.D.

**Educational Objectives:**
At the conclusion of this session, the participant should be able to evaluate efficacy and tolerability of long-term ziprasidone treatment in patients with bipolar disorder.

**Summary:**
We analyzed primary results from a two-year, open-label extension of a 21-day placebo-controlled trial of ziprasidone in mania associated with bipolar I disorder. Efficacy assessment were performed at day 3 and weeks 1, 2, 4, 12, 28, 52, 76, and 104. Observed cases and last visit (LOCF) analyses were conducted. The extension enrolled 127 patients. Mean dosage was 122.4 mg/day. A Kaplan-Meier survivor estimate found 50% of patients in the study at day 100 and 30% after one year. Scores of the Mani Rating Scale and CGI-S, the primary efficacy variables, continued to improve from extension baseline up to week 12, with improvement sustained at weeks 28, 52, 76, and 104, and last visit. Concomitant medications included anxiolytics (77.9%), hypnotics and sedatives (41.7%), antiepileptic drugs (29.9%), antidepressants (27.6%), and lithium (14.1%). Ziprasidone was well tolerated; 15 (11.8%) patients discontinued due to treatment-related adverse events. Twenty-five (12.5%) patients had weight gain 7% and 20 (17.9%) weight loss 7%.

Ziprasidone is associated with long-term symptom and global improvement in patients with bipolar I disorder and is well tolerated, with a weight-neutral profile.

**References:**

**NR746**
**Wednesday, May 5, 3:00 p.m.-5:00 p.m.**
**Aripiprazole for Relapse Prevention in Bipolar Disorder in a 26-Week Trial**

Paul E. Keck, Jr., M.D., Biological Psychiatry Department, University of Cincinnati, Medicine, 231 Albert Sabin Way, ML559, Cincinnati, OH 45267-0559; Raymond Sanchez, M.D., Ronald N. Marcus, M.D., William H. Carson, Jr., M.D., Linda Rollin, Ph.D., Taro Iwamoto, Ph.D., Elyse G. Stock, M.D.

**Educational Objectives:**
At the conclusion of this presentation, the participant should be able to understand the efficacy of aripiprazole for the maintenance treatment of bipolar I disorder.

**Summary:**
Objective: To compare aripiprazole with placebo in the maintenance of stability of patients with bipolar I disorder in a 26-week, double-blind relapse prevention study.

**Methods:** Patients who had recently experienced a manic or mixed episode, entered a stabilization phase receiving open-label aripiprazole 15–30 mg/day (starting dose = 30 mg/day), for 6–18 weeks. After meeting stabilization criteria (Y-MRS<10 and MADRS<13 for four consecutive visits or six weeks), 161 patients were randomized to aripiprazole or placebo for the 26-week maintenance phase. The primary endpoint was time to relapse of manic, mixed, or depressive symptoms, defined as discontinuation due to lack of efficacy (hospitalization for manic or depressive symptoms, or requiring a dosing change in psychotropic medications other than study drug).

**Results:** Time to relapse of symptoms was significantly prolonged with aripiprazole compared to placebo (p=0.020). Total number of relapses (manic, mixed, or depressive symptoms) were significantly fewer in patients treated with aripiprazole than placebo (25% vs. 43%, p=0.013). The only adverse events (≥10% incidence) more common than placebo were anxiety and nervousness.

**Conclusion:** Aripiprazole prolongs time to relapse of symptoms in stabilized patients with bipolar I disorder who previously experienced a manic or mixed episode.

**Funding Source(s):** Bristol-Myers Squibb Company and Otsuka Pharmaceutical Co., Ltd

**References:**
NR747

Wednesday, May 5, 3:00 p.m.-5:00 p.m.
CDN Network for Bipolar Disorder: Preliminary Report on Data From 139 Patients
Supported by Janssen-Ortho, Inc.

Lakshmi N. Yatham, M.B., Department of Psychiatry, University of British Columbia, 2255 Westbrook Mall, Vancouver, BC V6T 2A1, Canada; Peter Silverstone, M.D., David Mitenko, B.S.C., Sagar V. Parikh, M.D., Mark Lander, M.D., Terry Isamura, M.D., Roumen V. Milev, M.D., Philippe Baruch, M.D., Chris P. Gorman, M.D., Jean Leblanc, M.D., Pablo Cervantes, M.D., Serge Beaulieu, M.D., Verinder Sharma, M.D., Mary C. Connolly, M.D., Javed Ali, M.D.

Educational Objectives:

At the conclusion of this session, the participant should: (1) understand the long term course of bipolar disorder; (2) learn the effectiveness of various treatments commonly used for bipolar disorder; (3) recognize the predictors of response to various treatments.

Summary:

Objective: Understanding naturalistic treatment patterns and course in Bipolar Disorder.

Method: Prospective data was collected at 14 Canadian centers for patients diagnosed with bipolar I/II who had within the previous 3 months met criteria for a mood episode and required a change in treatment. Baseline data collected included psychiatric medications and behavioural symptom rating scales. Patients were managed utilizing routine clinical practice; behavioural scales were administered every 3 months. 198 enrolled; 139 met completer criteria.

Results: Of 139 patients, 99 (71%) were diagnosed with BD I; 40 (29%) with BD II. The most recent episode at baseline was depression [N=86 (62%) (Group 1)]; 53 (38%) had mania/hypomania [Group 2]. 66% of Group 1 relapsed within three months; 84% within six months. In Group 2, 63% relapsed within three months; 68% within six months. Mean number of relapses in both groups was higher in BD II patients than BD I (p<0.01). Initial results indicate the most commonly prescribed mood stabilizer was divalproex, bupropion was the most frequently prescribed antidepressant, and glazapine the most frequently prescribed antipsychotic.

Conclusion: Patients with a recent depressive episode are more likely to relapse within both 3 and 6 months than patients with a recent manic/hypomanic episode. Furthermore, BD II patients relapse more frequently than BD I patients and require close monitoring.

Research Funding has been provided in the form of unrestricted grants from Janssen-Ortho, Canada and The Lundbeck Institute (Canada/Denmark).

References:


NR748

Wednesday, May 5, 3:00 p.m.-5:00 p.m.
Topiramate Treats Mood Disorders in People With Developmental Disabilities
Supported by Ortho-McNeil Pharmaceuticals

Martin S. Wolfson, M.D., Jervis Clinic, New York State IBR, 1050 Forest Hill Road, Staten Island, NY 10304; Albert G. Pfadt, Ph.D., Nicole Manos, M.A.

Educational Objectives:

At the conclusion of this session, the participants should be able to recognize potential benefits and side effects of using topiramate as an adjunctive treatment for mood disorders in children and adults with developmental disabilities.

Summary:

Objective: We wanted to evaluate the effectiveness of topiramate to treat mood disorders in children and adults with developmental disabilities.

Method: This was an open-label, retrospective study of 64 individuals ages 4–57, with profound to mild mental retardation treated with topiramate in a community mental health clinic. Treatment was initiated based on clinical indications of a mood disorder, lack of adequate response to previous treatment, and caregiver consent. Topiramate was used as monotherapy in nine individuals and as an add-on treatment for 55, most of whom were taking additional mood stabilizers. Outcomes were evaluated retrospectively by assigning a Clinical Global Impression-Improvement score 12 months after the initiation of treatment based on a review of caregiver reports and available behavioral data. A CGI-I score of 1 or 2 (very much or much improved) was used to identify responders.

Results: Our scoring criteria identified 39 responders (60.9%). Nine of 12 individuals with Fragile X Syndrome (75%) were identified as responders. Topiramate was associated with few side effects at the doses prescribed.

Conclusion: Topiramate was effective and well tolerated. It should be considered as an adjunctive treatment for mood disorders in people with developmental disabilities.

Funding Source(s): Grant from Ortho-McNeil Pharmaceutical.

References:


NR749

Wednesday, May 5, 3:00 p.m.-5:00 p.m.
Trends in Pharmacologic Treatment for Patients With Bipolar Disorder: 1992–2002
Supported by Eli Lilly and Company

Leslie Cooper, Ph.D., Outcomes Research, Eli Lilly and Company, Lilly Research Laboratories, Indianapolis, IN 46285; Zhongyun Zhao, Ph.D., Baofan Zhu, Ph.D.

Educational Objectives:

At the conclusion of the presentation, participants should be able to describe recent prescribing practice in patients with bipolar disorder and differences in medication use among sub-types of bipolar disorder.

Summary:

Methods: A large claims database of insured individuals from 10/1992 to 9/2002 was analyzed to identify patients diagnosed with bipolar disorder (ICD9-CM: 296.4x–296.8x). Treatment regimens were examined for six-classes of psychotropics (antidepressants, mood-stabilizers, atypical and typical antipsychotics, anxiolytics and hypnotics).

Results: Of 13,407 patients, the percent untreated remained stable around 10% over the 10-year period. Among treated patients, about 65% received mood stabilizers and/or antidepressants. The two agents most frequently used were valproate (39.7%) and olanzapine (24.2%) in 2002. Overall, mood stabilizers
increased slightly from 59.5% to 64.2%, and atypical antipsychotics increased from 4.5% to 45.1% usage. Antidepressants and anxiolytics remained stable at around 65% and 50% respectively, although the products chosen shifted with new market introductions. Typical antipsychotics decreased from 34.5% to 12.4%, and hypnotics decreased from 13.2% to around 7% usage.

Conclusions: Although about two-thirds of patients with bipolar illness receive mood stabilizers, there continues to be opportunity for improvement in pharmacotherapy. It is also important to understand outcomes associated with changing treatment patterns for bipolar patients.

Funding Source(s): Funded by Eli Lilly and Company.

References:

NR750 Wednesday, May 5, 3:00 p.m.-5:00 p.m.
Prior Lithium Treatment as a Predictor of Response to Subsequent Mood Stabilizer Therapy
Supported by GlaxoSmithKline
Guy M. Goodwin, M.D., Department of Psychiatry, University of Oxford, The Warneford Hospital, Headington, Oxford OX3 7JX, United Kingdom; Frederick K. Goodwin, M.D., Robert A. Leadbetter, M.D., Gary Evoniuk, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the audience will have an understanding of the predictive value of previous lithium treatment on subsequent response to lithium or lamotrigine therapy.

Summary:
Introduction: Lithium continues to be the reference standard among mood stabilizers. Two large maintenance studies have been completed studying both lithium and the anticonvulsant mood stabilizer, lamotrigine, enrolling both recently depressed (GW605) or manic/hypomanic/mixed (GW606) outpatients.

Objective: This analysis examined whether previous lithium experience predicted subsequent response to lithium or lamotrigine in these studies.

Methods: 588 currently or recently symptomatic bipolar I patients (DSM-IV) were randomized to 18 months of double-blind monotherapy with lamotrigine (100–400mg/day), lithium (0.8–1.1mEq) or placebo. Efficacy outcomes (time from randomization until intervention for an emerging manic or depressive episode) were examined according to previous lithium treatment, of whom 237 (71%) reported clinical response. Among previous lithium responders, median survival from baseline to endpoint in MADRS scores were −19.1 and −18.4 for the escitalopram and sertraline groups, respectively. At endpoint, 75% and 70% of escitalopram and sertraline treated patients, respectively, were responders (>=50% improvement from baseline in mean MADRS scores). For patients who were severely depressed at baseline (baseline MADRS >= 30; N=92), mean changes from baseline to endpoint in MADRS scores were −22.4 and −20.4 for the escitalopram and sertraline groups, respectively. Both treatments were well tolerated, with only 2% to 4% of patients discontinuing prematurely due to adverse events.

Conclusion: Fixed dose escitalopram 10 mg/day was comparably effective to sertraline, optimally dosed within its therapeutic dose range of 50–200 mg/day.

Funding Source(s): GlaxoSmithKline

References:

NR752 Wednesday, May 5, 3:00 p.m.-5:00 p.m.
Efficacy of Quetiapine in Mania Associated With Bipolar Disorder
Supported by AstraZeneca Pharmaceuticals
Roger S. McIntyre, M.D., Department of Psychiatry, University of Toronto, 399 Bathurst Street, Toronto, ON M5T 2S8, Canada
NR753  Wednesday, May 5, 3:00 p.m.-5:00 p.m.
Effect of First-Degree Family History in College Students With Bipolar Disorder

Cecyia Nowakowska, M.D., Psychiatry Department, Stanford University, 401 Quarry Road, Stanford, CA 94305-5723; Anna Sapozhnikova, Rebecca A. Chandler, B.S., Andrea M. Alarcon, B.A., Po W. Wang, M.D., Wendy K. Marsh, M.D., Terence A. Ketter, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to: (1) recognize that quetiapine treatment of mania in bipolar disorder results in improvement of a broad range of mood symptoms; (2) select agents for the treatment of bipolar disorder that are efficacious and well tolerated.

Summary:
Objectives: To evaluate the efficacy of quetiapine in the treatment of mania.

Methods: Patients with bipolar I disorder (manic episode, DSM IV) received quetiapine alone (up to 800 mg/day; 12 weeks) or in combination with lithium (0.7–1.0 mEq/L) or divalproex (50–100 μg/mL) (3 or 6 weeks) in randomized, placebo-controlled, double-blind studies. Efficacy measures included Young Mania Rating Scale (YMRS), response (>/=50% decrease in YMRS score), and remission (YMRS </=12) rates.

Results: In a combined analysis of two studies, the change from baseline in YMRS score with quetiapine monotherapy was significantly greater than with placebo from Day 4 onward (P=0.021), and increased by Day 21 (P<0.001) and Day 84 (P<0.001). Quetiapine combination therapy also improved YMRS scores within the first week (P<0.05) and up to Day 21 (P=0.014). Compared with placebo, quetiapine monotherapy or combination therapy resulted in a significantly higher proportion of patients achieving response and remission, and significantly greater improvement in each item of the YMRS and psychotic symptoms at Day 21 and onward.

Conclusions: Quetiapine improves mania as early as Day 4 and offers first-line efficacy for the treatment of a broad range of mood symptoms.

Funding Source(s): AstraZeneca, Wilmington, Delaware, USA

References:

NR754  Wednesday, May 5, 3:00 p.m.-5:00 p.m.
Sustained Remission/Euthymia With Quetiapine Monotherapy for Bipolar Mania
Supported by AstraZeneca Pharmaceuticals

Bjorn Paulsson, M.D., Clinical Research and Development, AstraZeneca, Clinical Research and Development, Sodertalje (B238), Sodertalje S15185, Sweden; Martin W. Jones, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to: (1) evaluate the effectiveness of quetiapine monotherapy in achieving sustained remission/euthymia in patients with bipolar mania; (2) determine how different cut-off criteria impact the efficacy findings in placebo-controlled studies of quetiapine.

Summary:
Objectives: Determine the effectiveness of quetiapine in the treatment of mania using different criteria for clinical remission/euthymia.

Methods: Three cut-off criteria for remission/euthymia were used to analyze 12-week, randomized, double-blind, monotherapy data obtained from patients hospitalized with bipolar I mania who received quetiapine (up to 800 mg/day) or placebo in two studies of the same design.

Results: Mean YMRS scores at entry were 33.3 (n=208) and 33.5 (n=195) in the quetiapine and placebo groups, respectively. After three weeks, remission/euthymia rates with quetiapine monotherapy versus placebo were: 37.5% vs 23.1% (YMRS </=12); 35.6% vs 21.5% (YMRS /<12 + MADRS </=10); and 35.1% vs 20.0% (YMRS /<12 + MADRS /<8) (P < 0.01). After 3 months, rates of remission/euthymia versus placebo were: 65.4% vs 35.9% (YMRS /<12); 60.1% vs 30.8% (YMRS /<12 + MADRS /<10); and 58.7% vs 29.7% (YMRS /<12 + MADRS /<8) (P < 0.001). The average daily dose of quetiapine in responders was 575 and 598 mg at each assessment, respectively.

Conclusions: Quetiapine at a target dose of approximately 600 mg/day leads to significant improvements in the proportion of patients with mania achieving clinical remission/euthymia, regardless of the assessment criteria used. Meaningful improvements with quetiapine monotherapy are sustained for at least 3-months.

Funding Source(s): AstraZeneca, Wilmington, Delaware, USA
References:

NR755 Wednesday, May 5, 3:00 p.m.-5:00 p.m.
Using Mood State to Predict Polarity of Relapse in Bipolar Maintenance Studies
Supported by GlaxoSmithKline
Joseph R. Calabrese, M.D., Department of Psychiatry, University Hospital of Cleveland, 11400 Euclid Avenue, Suite 200, Cleveland, OH 44106; Charles L. Bowden, M.D., Eduard Vieta, M.D., Robert L. Finding, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to: (1) recognize that quetiapine is an effective and well tolerated treatment for bipolar depression and is not associated with treatment-emergent mania; and (2) understand that quetiapine treatment may improve a broad range of symptoms in patients with bipolar disorder.

Summary:
Objective: Evaluate efficacy and tolerability of quetiapine monotherapy for major depressive episodes in patients with bipolar disorder.

Method: 539 patients (358 bipolar 1, 181 bipolar II depression) randomized to eight weeks double-blind treatment with quetiapine (fixed dose 300 or 600 mg/d) or placebo. Primary endpoint: change from baseline to endpoint in Montgomery-Asberg Depression Rating Scale (MADRS) total score.

Results: Patients taking quetiapine 300 and 600 mg/d had a significantly (P<0.001) greater improvement in mean MADRS and HAMD scores vs placebo at every assessment starting with the first evaluation (Day 8) and sustained through endpoint (Week 8) (MADRS: −16.7 and −16.4 vs −10.2) (HAMD: −13.8 and −13.4 vs −8.5). Significantly (P<0.05) more quetiapine patients (both doses), vs placebo were considered responders (≥50% decrease from baseline MADRS score) from week 2 through the end of the study. Treatment-emergent mania did not differ between quetiapine and placebo (3% vs 4%). Common quetiapine adverse events (≥10% and ≥2x placebo rate) were dry mouth (43%), sedation (31%), somnolence (26%), dizziness (20%), and constipation (11%).

Conclusions: Quetiapine monotherapy (300 or 600 mg/d) is significantly more effective than placebo and well tolerated for the treatment of depressive episodes in patients with bipolar disorder.

References:

NR757 Wednesday, May 5, 3:00 p.m.-5:00 p.m.
Work Loss Associated With Bipolar Disorder
Supported by AstraZeneca Pharmaceuticals
Rahul M. Sasane, Ph.D., US Science Initiative, AstraZeneca, 221 S. High Point Road, Suite 211E, Madison, WI 53717; Gregory de Lissovoy, Ph.D., Louis Matza, Ph.D., Josephine Maukopf, M.D., Jacqueline Pesa, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to (1) evaluate costs associated with work loss due to bipolar disorder and unipolar depression; (2) recognize the significant burden of illness due to bipolar disorder and unipolar depression.

Summary:
Objective: To assess indirect costs of work loss associated with bipolar disorder and major (unipolar) depression.

Method: From MEDSTAT's employer-based MarketScan© database for 2000, workers (mean age 42 ± 9) with a primary ICD-9-CM diagnosis of bipolar disorder (N=740), major depression (N=...
6,314), and one-to-one matched controls with no psychiatric diagnosis were identified. Work loss parameters were absence hours and payments for short-term disability and worker compensation.

**Results:** Mean annual absence hours were 55 (± 149) for the bipolar group vs 21 (± 27) for controls (P=0.009), and 53 (± 154) for the unipolar depression group vs 24 (± 48) for controls (P<0.0001). Mean short-term disability payments were $1,231 (±3,424) for the bipolar group vs $131 (± 967) for controls (P<0.0001), and $741 (± 2,873) for the unipolar depression group vs $178 (± 1,309) for controls (P<0.0001). Mean worker compensation payments were $554 (±4,231) for the bipolar group vs $228 (±2,289) for controls (P=0.15), and $518 (± 4,814) for the unipolar depression group vs $220 (± 2,449) for controls (P=0.0001).

**Conclusions:** Bipolar disorder and major unipolar depression significantly increased work loss. Patients with bipolar disorder may exhaust their sick leave and go onto short-term disability more frequently than those with major depression.

**Funding Source(s):** AstraZeneca, Wilmington, Delaware, USA

**References:**

**NR759** Wednesday, May 5, 3:00 p.m.-5:00 p.m.

**Is Rapid Cycling a Predictor of Nonresponse to Lithium?**

Melvin D. Shelton III, M.D., Department of Psychiatry, Case Western School of Medicine, 11400 Euclid Avenue, Suite 200, Cleveland, OH 44106; Daniel J. Rapport, M.D., Eric A. Youngstrom, Ph.D., Omar Elhaj, M.D., Sarah R. Bilali, M.A., Robert L. Findling, M.D., Joseph R. Calabrese, M.D.

**Educational Objectives:**
To compare the long-term efficacy of lithium and divalproex monotherapies in relapse prevention

**Summary:**

**Methods:** A 20-month, double-blind, parallel group comparison was carried out in recently hypomanic/manic patients who experienced a bimodal response to combination treatment of lithium and divalproex. Patients were randomized to monotherapy in a balanced design after stratifying for bipolar type I and II.

**Results:** Of 254 enrolled into open stabilization, 28% were non-compliant, 25% non-responders (73% resistant depression and 27% resistant hypomania/mania), 24% randomized, and 19% had intolerable side effects. Of the 60 randomized, 53% relapsed (59% into depression and 41% into hypomania/mania), 22% completed, 10% had intolerable side effects, and 10% were non-compliant. The mood episode relapse rate was 56% on lithium and 50% on divalproex. The depression relapse rate was 34% on lithium and 29% on divalproex. The hypomania/mania relapse rate was 22% for both arms. Intolerable side effects were experienced by 16% on lithium and 4% on divalproex (ns). Median survival was 18 weeks on lithium and 45 weeks on divalproex (p=0.389).

**Conclusions:** Both lithium and divalproex are effective in the long-term management of rapid-cycling bipolar disorder.

**Funding Resource(s):** NIMH R01 50165, Stanley Medical Research Institute, study medications from Abbott Pharmaceuticals

**References:**

**NR760** Wednesday, May 5, 3:00 p.m.-5:00 p.m.

**Comorbidity of Psychiatric Disorders and Polycystic Ovarian Syndrome**

Arabelle Rassi, M.D., Institute of Psychiatry, Federal University Rio Janeiro, R. Visconde de Pirajá 407702, Rio de Janeiro, RJ
Treatment-Resistant Depression trial, 14 receiving 2.5 g/day of metformin (group 1), 12 taking 1.5 g/day (group 2), eight taking placebo (group 3) and 14 not medicated (group 4). We made psychiatric evaluations using the Mini International Neuropsychiatric Interview (MINI) on outpatients with ultrasound guided needle aspiration and suggests that it is the common pathological link of these exuberant clinical features have higher body mass index and insulin resistance. The level of body mass is related to insulin resistance and suggests that it is the common pathological link of these illnesses.

References:

NR762 Wednesday, May 5, 3:00 p.m.-5:00 p.m.
Patterns of Pharmacologic Treatment for Patients With Bipolar Disorder Supported by Eli Lilly and Company
Baojin Zhu, Ph.D., Outcomes Research, Eli Lilly and Company, Lilly Research Laboratories, Indianapolis, IN 46285, Zhongyun Zhao, Ph.D., Liesl Cooper, Ph.D.
Educational Objectives:
At the conclusion of the presentation, participants should be able to describe recent prescribing practice in patients with bipolar and differences in medication use among sub-types of bipolar disorder.

Summary:
Objective: Assess recent pharmacologic treatment patterns for patients with bipolar disorder.
Methods: A large claims database of insured individuals from 10/1998 to 9/2002 was analyzed to identify patients diagnosed with bipolar disorder (ICD-9-CM: 296.4x-296.8x). Treatment regimens were examined for six classes of psychotropics (antidepressants, mood stabilizers, atypical and typical antipsychotics, anxiolytics and hypnotics) during the year post-diagnosis. Differences in medication use among subtypes of bipolar were compared.

Results: Of 6,373 patients (56.4% female, mean age 49.2 years), 19.4% were depressed, 14.2% manic, 21.2% mixed, and 45.1% other episodes; 9.1% didn’t receive psychotropic treatment. Among treated patients, 66.0% received antidepressants, 64.0% mood stabilizers, 48.2% anxiolytics, and 42.1% atypical antipsychotics. Valporate (40.3%) and olanzapine (22.0%) were top two classes of psychotropics. Depressed patients were more likely to receive antidepressants and anxiolytics but less likely to receive mood stabilizers.

NR761 Wednesday, May 5, 3:00 p.m.-5:00 p.m.
A Long-Term, Prospective, Naturalistic Study of Usual Standard-of-Care Treatment in Patients With Treatment-Resistant Depression Supported by Cyberonics, Inc.
David L. Dunner, M.D., Department of Psychiatry, University of Washington, 4225 Roosevelt Way NE, 306C, Seattle, WA 98105-6099
Educational Objectives:
At the conclusion of this session, the participant should be able to recognize clinical characteristics of TRD and understand the difficulty in treating this population, despite the wide range of treatment options.

Summary:
Background: This prospective and naturalistic study evaluates the clinical outcomes and cost utilization among patients with treatment-resistant depression (TRD) who are treated in accordance with the current standard of care.

Methods: 13 clinical sites participated in this study. Enrolled patients met DSM-IV criteria for a current major depressive episode (MDE) of at least two years in duration and/or had a history of recurrent MDEs. Patients must not have had an acceptable clinical response to at least two treatments (medication and/or ECT) during the current MDE. Usual standard-of-care was defined as any treatment strategy that the patient and physician chose to follow. Assessments included the IDS-SR25, HRSD24, quality of life, and healthcare utilization.

Results: 127 patients enrolled in the study at 13 U.S. centers. Mean age was 46 years and 69% were female. Average duration of the current episode was six years, average length of illness was 25 years. Mean total number of unsuccessful antidepressant medication trials during the current episode was 3.5. Response was defined as a ≥50% improvement on the IDS-SR25 and HRSD24. Data on 112 patients at one year show response rates of 11.6% and 12.5% for the IDS-SR and HRSD24, respectively and only 5% (5/112) were considered sustained responders (≥50% improvement in IDS-SR at both nine and 12 months).

Conclusions: One-year data suggests that current psychiatric management in patients with TRD is less than optimal.

Funding Source(s): Grant support provided by Cyberonics, Inc.
References:


NR763 Wednesday, May 5, 3:00 p.m.-5:00 p.m.

Estimating Depression Prevalence With the BDI: Is Seasonal Mood Variation a Confound?

Erin E. Michalak, Ph.D., Department of Psychiatry, University of British Columbia, 2255 Wesbrook Mall, Vancouver, BC VGT 2A1, Canada; Greg Murray, Ph.D., Chris Duvrick, M.D., Clare Wilkinson, M.D., Lourdes Lasa, M.D., Ville Lehtinen, M.D., Odd S. Dalgard, M.D.

Educational Objectives:

At the conclusion of this session, the participant should: (1) have an understanding of the relationship between seasonality and depressive symptomatology; (2) recognize that seasonality is a potential confound in estimates of depression prevalence; (3) Learn that season of administration does not appear to confound estimates of depression prevalence made via the BDI.

Summary:

Objectives: The existence of winter seasonal affective disorder (SAD) and its milder population variants implies that depression estimates in a given population may be higher in winter than at other times of the year. The aim of the present study was therefore to test whether depression prevalence estimates based on the Beck Depression Inventory (BDI) are systematically confounded by season of administration.

Method: Existing information from the screening phase of a multicentre investigation of depression prevalence provided the data for the study. Repeated cross-sectional BDI data from samples in the United Kingdom (N = 1299), Finland (N = 1352), Norway (N = 2711) and Spain (N = 1246) were analysed for month- and season-of-administration effects.

Results: Whether measured continuously, or as a dichotomous variable (BDI cut-off ≥ 13), there was no evidence of a systematic seasonal pattern in depression estimates across the four sites. No seasonal effects reached statistical significance at any single site, and trends in the association between winter and elevated BDI scores were positive in two sites (UK and Norway) and negative in two (Finland and Spain).

Conclusion: Although limited by a posthoc analysis of existing data, the present study provides the strongest evidence to date that season of administration is not a confound of depression prevalence as estimated by the BDI.

Funding Source(s): EC Biomed 2; NHS Executive Northwest Research and Development Office; Spanish Fondo de Investigación Sanitaria; Wales Office of Research and Development; Norwegian Research Council; Finnish Pensions Institute.

References:


NR764 Wednesday, May 5, 3:00 p.m.-5:00 p.m.

Depressive Symptoms and Self-Care in Persons With Diabetes

Daniel P. Chapman, Ph.D., Health and Aging Branch, Center for Disease Control, 4770 Buford Highway N.E., MS K45, Atlanta, GA 30341; Matthew M. Zack, M.D., Michelle D. Owens, Ph.D., Ping Zhang, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to describe the relationship between depressive symptoms and a variety of health behaviors among persons with diabetes.

Summary:

Objectives: Previous research has established an increased prevalence of depressive symptoms among persons with diabetes relative to their non-diabetic peers and depression is associated with impaired glycemic control. As self-care behaviors have been posited to mediate the relationship between depression and glycemic control, we investigate the association between depressive symptoms and a variety of health behaviors among persons with diabetes residing in the community.

Methods: Data for this investigation were obtained from adult community-dwellers who responded to the 2001 Behavioral Risk Factor Surveillance System, a telephone survey assessing behavioral and health characteristics. Respondents estimated the number of days during the past 30 days when they felt depressed, as well as reporting if a doctor had ever told them they had diabetes. Germane measures of self-care were assessed, as were health behavior necessitating consultation with health care providers.

Results: Frequent depressive symptoms were not associated with significant differences in the likelihood of consultation with health care providers (eye or foot examinations, influenza or pneumonia vaccinations). However, frequent depressive symptoms were associated with both physical inactivity among men with diabetes and an increased probability of a body mass index of 30 or greater among diabetic women.

Conclusions: These data suggest assessment of depressive symptoms may alert clinicians to potential self-care deficits which may prove deleterious to the health of persons with diabetes.

References:


NR765 Wednesday, May 5, 3:00 p.m.-5:00 p.m.

The Prophylactic Efficacy of SSRI's

Eric D. Peselow, M.D., Department of Psychiatry, New York University School of Medicine, 32 Bassett Avenue, Brooklyn, NY 11234; Mary Anne Pressman, M.D., Mary T. Guardino, B.A.

Educational Objectives:

To evaluate the probability of remaining stable on one of four SSRI's that the patient had initially responded to over a five year continuation period to assess the efficacy and need for long-term treatment.

Summary:

Objective: The long-term efficacy of selective serotonin reuptake inhibitors (SSRIs) in preventing recurrent episodes of depression after successful treatment of the acute episode has not been shown for > 2 years in controlled trials or naturalistic studies. The purpose of this study is to evaluate the prophylactic efficacy of four SSRIs: fluoxetine, citalopram, sertraline, and paroxetine in a
naturalistic clinical setting to responders to these medicines during acute depression who continued on the medications for six months to ten years.

**Method:** 256 patients who were acutely treated for depression with one of the four SSRI's and were continued on the medication to which they responded, were followed from their seventh month of euthymic mood until a well defined termination or a recurrence of depression (meeting DSM-IV criteria for major depression) causing a medical decision to reinstitute medication.

**Results:** Despite receiving SSRI medication prophylactically at a dose to which they had responded acutely, 41% (105/256) suffered a recurrence of depression. The one, three and five year probability of remaining free of a depressive episode was 87%, 67% and 48% respectively.

**Conclusion:** In a naturalistic setting, long-term treatment with antidepressants still yielded substantial relapse. There was no funding for this study.

**References:**

**NR767 Wednesday, May 5, 3:00 p.m.-5:00 p.m.**

Relapse of Depression During Pregnancy Following Discontinuation of Antidepressant Treatment

Lee S. Cohen, M.D., Department of Psychiatry, MGH Center for Women's Health, 15 Parkman Street, WAC 812, Boston, MA 02114; Lori L. Alshuler, M.D., Zachary N. Stowe, M.D., Ruta M. Nonacs, M.D., Rita Suri, M.D., D. Jeffrey Newport, M.D., Bernard L. Harlow, Ph.D.

**Educational Objectives:**
At the conclusion of this session, the participant will appreciate the risk for relapse associated with antidepressant discontinuation during pregnancy.

**Summary:**
**Objective:** The current study evaluated the risk for relapse in euthymic women who either discontinued or maintained antidepressant treatment across pregnancy.

**Methods:** Two hundred and fifty pregnant women with a history of major depression were enrolled in a prospective study with monthly follow up appointments throughout pregnancy using structured clinical instruments. All subjects were euthymic for at least three months prior to and at conception. The group was stratified based on decisions regarding antidepressant treatment from three months prior to conception to 16 weeks gestation: (1) discontinued or lowered antidepressant daily dose for at least one week or (2) maintained antidepressant therapy throughout pregnancy. In this preliminary analysis, we compared the results from the first 103 enrolled study subjects who either discontinued or maintained antidepressant therapy.

**Results:** Subjects who discontinued antidepressants were 3.6 times more likely to experience relapse of major depression during pregnancy compared with those who maintained antidepressant treatment (95% CI 1.9–6.8).

**Conclusion:** These preliminary findings suggest that discontinuation of antidepressant treatment during pregnancy is associated with a significant risk for relapse compared to continuation of pharmacotherapy. Results from this prospective study will assist clinicians in assessing the risks and benefits associated with treatment of major depression during pregnancy. Outcome of infants whose mothers who either continued or maintained antidepressant treatment is currently being analyzed.

**Funding Source(s):** Multi-institutional collaborative RO1 from the National Institute of Mental Health (MH# 56420-05).

**References:**

**NR768 Wednesday, May 5, 3:00 p.m.-5:00 p.m.**

Perimenopause and Risk for Depression: The Harvard Study of Moods and Cycles

Lee S. Cohen, M.D., Department of Psychiatry, MGH Center for Women's Health, 15 Parkman Street, WAC 812, Boston,
At the conclusion of this session, the participant will recognize the heightened vulnerability for depression in women during the menopausal transition, and the potential health implications of this increased risk.

**Summary:**

**Background:** The existence of an association between depression and menopause has been investigated for more than a century. However, descriptions of a "perimenopausal depressive syndrome" have derived from studies with inconclusive findings and methodologic inconsistencies.

**Objective:** To examine the association between menopausal transition and first onset of depression.

**Methods:** The Harvard Study of Moods and Cycles is a population-based study in which over 4,000 premenopausal women (aged 36 to 44) were sampled to examine the association between a history of major depression and declining ovarian function. In the current study, we describe outcome following prospective assessment of 644 women with no history of depression who were followed with respect to associated risk for developing first onset of depression during the transition to menopause. Subjects had menstrual and psychiatric status were carefully assessed over time using a menstrual history questionnaire, Center for Epidemiologic Studies of Depression (CES-D scores), and Structured Clinical Interviews for DSM-IV (SCID) for depression history confirmation.

**Results:** Premenopausal women with no lifetime history of major depression who enter the perimenopause (N=365) were three times more likely to develop depressive symptoms than women of similar ages who remain premenopausal (N=228) (OR=3.2, CI=1.6–6.1). The strength of this association increased with greater numbers of adverse life events. In addition, there appeared to be an intensification of risk for depression in women who approached the menopause with significant vasomotor symptoms (OR=6.4, CI=3.9–13.8).

**Conclusions:** The transition to menopause may represent a period of heightened risk for first onset of depression and its attendant morbidity.

**Funding Source(s):** NIMH

**References:**


**NR770**

**Wednesday, May 5, 3:00 p.m.-5:00 p.m.**

**Linear Relationship of Serum Valproate Level to Response in Mania**

**Supported by Abbott Laboratories**

Michael H. Allen, M.D., Department of Psychiatry, University of Colorado, North Pavilion, 4455 E. 12th Avenue, #A011-95, Denver, CO 80220; Jeff Baker, Ph.D., Patricia J. Wozniak, Ph.D.

**Educational Objectives:**

At the conclusion of this session, the participant should be able to describe the dose response relationship of divalproex sodium in mania and identify blood levels associated with the greatest reduction in manic symptoms.

**Summary:**

**Introduction:** Valproate (VPA) serum levels below 50 are less effective and levels above 125 are more often toxic but, beyond that, there is little evidence to guide dosage in acute mania. The authors hypothesized a linear relationship of serum level to response with higher levels more effective than lower levels.

**Design:** We performed a post hoc analysis of pooled intent-to-treat data from three randomized, fixed dose, placebo-controlled studies of divalproex for acute mania. Subjects (N=374) were stratified into a placebo group and six serum VPA ranges and effect size was determined for each serum level range. Linearity of dose response was tested with both parametric (linear regression) and nonparametric (Jonckheere-Terpstra) techniques with and without the placebo group. ANOVA was used to compare the response of subjects in each range with those in the lowest active drug range and the placebo group. The mean serum VPA level was then determined for all subjects with an effect greater than or equal to the maximal effect derived from linear modeling.

**Results:** Dose response fit a linear model with placebo (slope $p<.001$, fitness $=0.873$, Jonckheere $p<.001$) and, more conservatively, without placebo (slope $p=.007$, fitness $=0.757$, Jonckheere...
In the ANOVA comparing the five higher serum VPA groups with the lowest serum VPA group and placebo, efficacy was significantly greater than placebo beginning at the 71–85 μg/ml range (p=0.021) and for all higher VPA levels. The 94–107 and >107 μg/ml groups were also superior to the lowest VPA group, ≤55 μg/ml, median 41 μg/ml (p=0.012) The effect size for the 94–107 and the >107 μg/ml strata was a robust −1.06 and −1.07 respectively, equivalent to a decrease of approximately 12 points on the YMRS. Using an effect size of −1.1 derived from linear modeling as an estimate of maximal effect, we examined all subjects meeting that response criterion (n=84) and found a median blood level of 87 μg/ml associated with that response.

**Conclusion:** If tolerated, VPA levels of approximately 90 μg/ml or higher appear to offer greater efficacy.

**Funding Source(s):** Abbott Laboratories

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**References:**


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**NR771 Wednesday, May 5, 3:00 p.m.-5:00 p.m.**

**Do Antidepressants Improve Long-Term Mood Morbidity in Bipolar Disorder?**

S. Nassir Ghaemi, M.D., Department of Psychiatry, Cambridge Street, Cambridge, MA 02139; Rif S. El-Mallakh, M.D., Claudia F. Baldassano, M.D., Michael J. Ostacher, M.D., Gary S. Sachs, M.D., Frederick K. Goodwin, M.D., Ross J. Baldessarini, M.D., M.D.

**Educational Objectives:**

At the conclusion of this session, the participant should be able to determine if long-term antidepressant use reduces affective morbidity in bipolar disorder.

**Summary:**

**Objective:** Previous studies suggest that TCAs may worsen the course of bipolar disorder (1), or may be ineffective in bipolar depressive prophylaxis. Many believe modern antidepressants are more effective and safe. This is the first randomized study of long-term outcome in bipolar disorder with modern antidepressants.

**Method:** In interim analysis at halfway point of 5-year study (n=33), subjects first recovered from a depressive episode on mood stabilizer plus antidepressant were openly randomized to continue (LT; n=14) or discontinue (ST; n=19) antidepressants (up to one-year follow-up presented). Primary outcome was affective morbidity measures in the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) study.

**Results:** ST group had slight benefit over LT group in a repeated measures linear regression model (adjusted for rapid cycling, gender, substance abuse, psychosis, antidepressant attitude) (β= −0.40; 95% CI [-2.21, 1.42]). ST group had less morbidity regardless of rapid cycling status. Magnitude of decreased morbidity was higher in non-rapid cycling (β=−2.62, 95% CI [-5.17, −0.06]; p=0.05) versus rapid cycling (β=0.71, 95% CI [-4.45, 3.03]; NS).

**Conclusions:** These data are consistent with either non-inferiority or slight superiority of antidepressant discontinuation compared with antidepressant continuation. Antidepressant use even appeared harmful in non-rapid cycling bipolar disorder. Modern antidepressants may not be more effective or safer than TCAs in bipolar disorder.

**Funding Source(s):** NIMH grant MH-64189-03

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**References:**


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**NR772 Wednesday, May 5, 3:00 p.m.-5:00 p.m.**

**Efficacy of Transcranial Magnetic Stimulation in Severe Major Depression**

Magali Benhaim-Moncoucy, M.D., Psychiatry Department, Université Hospital, Rue du General Koenig, Reims Cedex 51092, France; Charles S. Peretti, M.D., Florian Ferreri, M.D., Fabien Gierski

**Educational Objectives:**

This poster will help students to learn about rTMS indications in psychiatry, mainly in depression.

**Summary:**

**Objective:** The study aim was to compare the antidepressant efficacy of treatment with low frequency rTMS alone, with the rTMS-paroxetine association, and with clomipramine, in patients with major depressive episodes of acute severity.

**Methods:** Twelve inpatients suffering from major depression of acute severity (HDRS-21 items score ≥ 26) were randomized in three groups of treatment, respectively: rTMS, rTMS-paroxetine and clomipramine. Stimulation parameters were: Frequency: 1Hz, Intensity: 110% of the motor threshold, Train duration: 60s, Inter-train interval: 180s, two trains per session, 10 sessions per week over a 10-day period, with a total of 12,000 stimuli. HDRS, MADRS and CGI were used to assess antidepressant efficacy weekly over a 6 weeks treatment period.

**Results:** At D14 depression scales mean scores were inferior in the rTMS group to that of the clomipramine group (p=ns). CGI mean score were lower in the rTMS group, and the rTMS-paroxetine group at D14 and a superior efficacy/tolerance ratio from D14 to D42.

**Conclusion:** The preliminary results suggest a therapeutic efficacy of rTMS similar to that of clomipramine with a shorter reaction time to rTMS. Finally, a tendency to better tolerance can be observed in the group treated with rTMS.

**References:**


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**NR773 Wednesday, May 5, 3:00 p.m.-5:00 p.m.**

**Double-Blind Comparison of Escitalopram and Venlafaxine Extended Release in the Treatment of MDD**

**Supported by Forest Laboratories, Inc.**

Robert J. Bielski, M.D., Health Department, Summit Research Net. Institute, 4084 Okemos Road, Suite A, Okemos, MI 48864-3258; Daniel Ventura, Ph.D., Chung-Chi Chang, Ph.D.
Educational Objectives:

At the conclusion of this session, the participant should be able to evaluate the relative efficacy and tolerability of escitalopram 20 mg/day compared with venlafaxine XR 225 mg/day.

Summary:

Objective: A previous flexible-dose study compared escitalopram 10–20 mg/day with venlafaxine XR 75–150 mg/day, and demonstrated that escitalopram is at least as effective as venlafaxine XR, and better tolerated. This report compares these compounds in depressed outpatients at the highest doses recommended in the U.S.

Methods: In this randomized trial, patients presenting with a DSM-IV-defined episode of major depressive disorder (baseline HAMD >= 20) received one week of single-blind placebo treatment, followed by eight weeks of double-blind fixed-dose treatment with either escitalopram or venlafaxine XR (titrated to 20 mg/day and 225 mg/day, respectively, in accordance with prescribing information). Mean change from baseline to endpoint in MADRS scores was the primary efficacy variable. Remission was defined as MADRS score <= 10. Response was defined as at least a 50% reduction from baseline MADRS scores.

Results: Mean baseline MADRS scores for the escitalopram (N=97) and venlafaxine (N=98) groups were 30.7 and 30.0, respectively, indicative of moderate to severe illness. Escitalopram appeared to be at least as effective as venlafaxine XR, with mean changes in MADRS scores from baseline to endpoint of -15.9 and -13.6, respectively (p=0.12). Remission rates at endpoint were 41.2% for escitalopram and 36.7% for venlafaxine. Response rates were 58.8% and 48.0% for escitalopram and venlafaxine XR, respectively. Tolerability measures favored escitalopram over venlafaxine treatment. Significantly more patients withdrew prematurely due to adverse events from the venlafaxine XR group (16.0%) than the escitalopram group (4.1%), p < 0.01.

Conclusion: These results demonstrate that escitalopram has a better risk/benefit profile than venlafaxine XR in the treatment of depression, and do not support the hypothesis that “dual action” agents have greater efficacy.

Funding Source(s): Forest Laboratories, Inc.

References:


NR774 Wednesday, May 5, 3:00 p.m.–5:00 p.m.
Analysis of the Hamilton Rating Scale for Depression in Dysthymic Disorder
Ruben A. Miozzo, M.D., Psychiatry Department, Umass Medical School, 55 Lake Avenue North, Worcester, MA 01655; Sarai Batchelder, Ph.D., Mayra Tisminetzky, M.D. David J. Hellerstein, M.D.

Educational Objectives:

At the conclusion of this session, the participant should recognize the presence of a specific pattern of symptoms in patients with dysthymic disorder.

Summary:

Purpose: To determine whether dysthymic disorder (DD) presents a specific symptom-pattern on the Hamilton Rating Scale for Depression (HRSD). We will replicate previously reported factor analysis for neurotic depression to compare the clustering of HRSD items in both conditions.

Background: The inclusion of DD in the DSM-III replaced the constructs of neurotic depression (ND), depressive personality, and chronic depression. Controversy emerged as to whether the three heterogeneous diagnoses were suitably subsumed by the DD construct, especially as these included chronic states of depression and conditions previously associated with neurotic or personality disorders. Clearly and Guy (1977) reported a factor structure for HRSD-21 scores in ND patients.

Methods: HRSD-21 scores were obtained in 156 outpatients (Mean age: 41.8+/–10.2 M/F:92/74) with DSM diagnosis of DD. Confirmatory factor analysis using LISREL was done to replicate a previously reported factor structure in ND patients.

Results: Our results failed to confirm previously reported factor structure. Relatively low internal consistency (Alpha: 0.58), and inter-item correlations were found.

Conclusions: The lack of confirmation may be due to low sensitivity of the HRSD to the symptoms of DD, differences between ND and DD diagnostic criteria, or lack of significant variability in the data.

Funding Source(s): This present research was done without any commercial support

References:


NR775 Wednesday, May 5, 3:00 p.m.–5:00 p.m.
Correlation Between CDS and PANSS in Depressed and Nondepressed Outpatients With Schizophrenia
Nael Kilzieh, M.D., VAPSHCS, American Lake Division 116-M, Tacoma, WA 98493; Kent S. Rosengren, M.A., Annette Kennedy, Psy.D., Nandan Kumar, M.D., Amanda Wood, Ph.D., Andre Tapp, M.D.

Educational Objectives:

At the conclusion of this session, participants will recognize the effectiveness of the CDS in discriminating between depression, negative symptoms, and EPS in stable schizophrenic outpatients. Participants will also understand the role of depression status as a confounding factor that explains inconsistencies in the literature.

Summary:

Introduction: The Calgary Depression Scale (CDS), compared with other measures of depression in schizophrenia, has less overlap with depressive, negative, and extra-pyramidal symptoms (EPS). However, these findings have been inconsistent. Current literature includes mixed inpatients, outpatients, depressed, and non-depressed samples. We examined these potential confounding factors by comparing depressed and non-depressed stable outpatients with schizophrenia and schizoaffective disorder.

Method: Outpatients (N = 25) were assessed using the CDS, Positive and Negative Syndrome Scale (PANSS), and Simpson Angus Scale (SAS) for EPS.

Results: The sample was divided into depressed (N = 10, CDS > 6) and non-depressed (N = 15, CDS ≤6) patients. No correlation was found between the CDS and PANSS (total, general, negative and positive subscales) or SAS scores in the depressed group. However, there were correlations between the CDS and PANSS total (r = 0.55, p = 0.03) and general subscale (r = 0.52, p = 0.05) in the non-depressed group.

Conclusion: The CDS is effective in discriminating between depression, negative symptoms and EPS in depressed stable outpatients with schizophrenia and schizoaffective disorder. Cor-
relation between the CDS and PANSS in non-depressed subjects implicates depression status as a potential confounding factor. Interpretation of existing and future results should take this finding into account.

References:

NR776  Wednesday, May 5, 3:00 p.m.–5:00 p.m.  
Placebo-Level EPS and Akathisia During Quetiapine Treatment for Mania  
Supported by AstraZeneca Pharmaceuticals  

Henry A. Nasrallah, M.D., Department of Psychiatry, University of Cincinnati Medical Center, 231 Albert Sabin Way, P.O. Box 670359, Cincinnati, OH 45267-0559  

Educational Objectives:
At the conclusion of this session, the participant should be able to: (1) calculate the akathisia level associated with the use of quetiapine for the treatment of mania in bipolar disorder; and (2) select agents for the treatment of bipolar disorder that are efficacious, well tolerated and likely to be accepted by patients using evidence-based principles.

Summary:
Objectives: Examine the incidence of EPS-related adverse events (including akathisia) during treatment with quetiapine for bipolar mania.

Methods: Patients with bipolar I mania treated with quetiapine (up to 800 mg/d as monotherapy or in combination with lithium [0.7 mEq/L] or divalproex [50–100 mg/mL]) in placebo-controlled, double-blind studies of up to 12 weeks duration. Adverse event reports and Simpson Angus Scale (SAS) and Barnes Akathasia Rating Scale (BARS) scores were outcome measures.

Results: EPS-related adverse events (including akathisia) with quetiapine monotherapy (12.9%) were no different than placebo (13.1%). Similarly, EPS-related adverse events with quetiapine plus lithium or divalproex (21.9%) were no different from lithium or divalproex monotherapy (19.2%). The incidence of akathisia was lower with quetiapine monotherapy than placebo (3.3% vs 6.1%), as it was with quetiapine combination therapy compared to lithium or divalproex monotherapy (3.6% vs 4.9%). No significant differences were observed between groups in SAS and BARS scores from baseline to endpoint. Anticholinergic use, a marker for EPS, was low in both groups.

Conclusion: The incidence of EPS and akathisia during quetiapine therapy for bipolar mania is no different from placebo. Avoiding EPS (including akathisia) enhances the tolerability and acceptability of treatment, which is of particular importance for patients with bipolar disorder.

Funding Source(s): AstraZeneca.

References:

NR777  Wednesday, May 5, 3:00 p.m.–5:00 p.m.  
Ziprasidone in Bipolar Mania: Efficacy Across Patient Subgroups  
Supported by Pfizer Inc.  

Steven G. Potkin, M.D., Department of Psychiatry and Human Behavior, University of California, Irvine, Robert Sprague. Director of Brain Imaging Ctr, Irvine, CA 92697-3960; Paul E. Keck, Jr., M.D., Earl Giller, Jr., M.D., Kathleen Ice, Ph.D., Lewis Warrington, Ph.D., Judith Dunn, Ph.D.

Educational Objectives:
At the conclusion of this presentation, participants should be able to: (1) identify clinically defined patient subgroups relevant to pharmacotherapy of mania associated with bipolar disorder; (2) and should be able to discuss the reported pooled and subgroup analyses from two 21-day, placebo-controlled trials of ziprasidone.

Summary:
Objective: To evaluate the efficacy of ziprasidone in bipolar mania, focusing on clinically relevant subgroups.

Methods: This was a secondary analysis of two randomized, double-blind, 21-day trials comparing flexible-dose ziprasidone (40–80 mg BID) with placebo in adults with mania associated with bipolar I disorder. Changes in Mania Rating Scale (MRS) and CGI-S were calculated for combined study populations and in subgroups of patients with manic episodes, mixed episodes, and with or without psychotic symptoms.

Results: Mean daily dose was approximately 120 mg. At last visit (LOCF), mean change in MRS in patients receiving ziprasidone (n=268) was −11.72 (baseline 26.82) versus −6.69 (baseline 26.53) in patients receiving placebo (n=131) (p<0.001). Change in CGI-S for ziprasidone was −1.19 (baseline 4.71) versus −0.66 (baseline 4.76) for placebo (p<0.001). Significant improvement versus placebo was observed from Day 2 for MRS and Day 4 for CGI-S. The 95% confidence intervals for placebo-corrected LS mean change from baseline in all patients and in the four subgroups (manic, mixed, and with and without psychotic symptoms) overlapped, indicating comparable efficacy.

Conclusions: Ziprasidone rapidly improves symptoms and global illness severity in bipolar mania and is efficacious in mixed and manic episodes and in presence or absence of psychotic symptoms.

Funding Source(s): Pfizer, Inc.

References:

NR778  Wednesday, May 5, 3:00 p.m.–5:00 p.m.  
Cultural Views Affect the Assessment of Manic Symptoms  
Supported by Pharmstar LLC  

Steven D. Targum, M.D., Steven G. Potkin, M.D., Pharmastar, 1488 Baltimore Pike, Springfield, PA 19064; Allen H. Young, M.D., Amir H. Kalaí, M.D., Dror Rom, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize that inter-cultural differences and interpretative biases may affect inter-rater agreement on some well established, reliable,
and valid psychiatric rating instruments (e.g., YMRS for manic symptoms).

Summary:
Rating instruments used to assess the severity of manic symptoms in bipolar patients can have broad applicability in both clinical practice and clinical trials to evaluate clinical change over time. The reliability and validity of these instruments is typically established in patient populations from the geographic locale of the scale developers. For instance, the Young Mania Rating Scale (YMRS) was developed using American manic patients from New York State. Global studies using raters from diverse geographical areas and cultures may encounter inter-cultural biases that affect inter-rater agreement. In this study, two YMRS videotaped interviews of American manic patients were shown to trained raters from three English language speaking countries (United States (82), United Kingdom (20), and India (24)). Total YMRS scores differed significantly between the U.S. and U.K. (p < 0.001), India and U.K. (p < 0.001), and the U.S. and Indian rater Groups (p = 0.004). Significant differences were revealed on 10 of the 11 YMRS items. The most profound differences were noted for mood elevation, irritability, thought content, and disruptive-aggressive behavior. These significant differences reflect distinct cultural biases regarding the interpretation of severity of manic symptoms and behavior.

Funding Source(s): Pharmastar LLC

References:

NR779 Wednesday, May 5, 3:00 p.m.–5:00 p.m.
Aripiprazole Augmentation in Treatment-Resistant Depression
Supported by Bristol-Meyers-Squibb and Otsuka Pharmaceutical Co., Ltd.

James G. Barbee IV, M.D., Psychiatry Department, LSUHSC, 1542 Tulane Ave, New Orleans, LA 70112-2825; Erich J. Conrad, M.D., Nowal Jaber-Jamhour, M.A.

Educational Objectives:
At the conclusion of this session, the participant should be able to assess the efficacy of aripiprazole in augmenting antidepressant treatment in non-psychotic treatment-resistant unipolar depression.

Summary:
Objective: To determine the efficacy of aripiprazole, a dopamine and 5HT1A partial agonist in augmenting antidepressant treatment in non-psychotic treatment-resistant unipolar depression.

Methods: A retrospective efficacy analysis was conducted in 30 treatment-resistant unipolar depressed patients with documented failure to ≥1 atypical (risperidone, olanzapine, quetiapine or ziprasidone) and who received antidepressant augmentation with aripiprazole. Prospectively documented CGI-1 and GAF scores were available for all patients and response was defined as a CGI-1 of 1 or 2 (very much or much improved).

Results: Following treatment with aripiprazole, 46.7% (14/30) of patients in the intent-to-treat analysis responded. The mean time to obtain a response was 3.10 weeks. The mean dose among responders was 13.0 mg/day. There appeared to be no relationship between response to aripiprazole and the number of prior failed atypical neuroleptic trials. The most commonly reported adverse events during augmentation with aripiprazole were insomnia, restlessness, headache, tremor, nausea, and sedation.

Conclusion: Aripiprazole was efficacious in improving response when given with antidepressants in highly treatment-resistant depressed patients who had failed at least one prior augmentation trial with another atypical antipsychotic. Further research is warranted to establish aripiprazole as a viable augmentation strategy for this difficult patient population.

Funding Source(s): Bristol-Myers Squibb Company and Otsuka Pharmaceutical Co., Ltd.

References:

NR780 Wednesday, May 5, 3:00 p.m.–5:00 p.m.
IM Ziprasidone in Agitated Psychotic Patients
Supported by Pfizer Inc.

David G. Daniel, M.D., Bioniche Development, PO Box 6207, McLean, VA 22106-7137; Shlomo Brook, M.D., Lewis Warrington, Ph.D., Antony D. Loebel, M.D., Stephen R. Murray, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to discuss the utility of IM ziprasidone for the treatment of an important subgroup of agitated and psychotic patients—patients with bipolar disorder diagnoses or schizoaffective disorder bipolar type.

Summary:
Objective: To evaluate the efficacy of IM ziprasidone in psychotic agitated patients with bipolar disorder or schizoaffective disorder bipolar type.

Methods: This was a subgroup analysis of two similarly designed, randomized, double-blind, fixed-dose, 24-hour studies of IM ziprasidone in agitated psychotic patients. Patients received 2mg control dose (n=15) vs 10mg (n=20) and 2mg (n=11) vs 20mg (n=15) (80mg maximum). Efficacy was assessed by Behavioral Activity Rating Scale (BARS), CGI-S, and PANSS Total and Agitation scores.

Results: The greatest reductions in agitation (mean change in BARS) at 2h and 4h post-first-dose were seen with 20-mg IM ziprasidone. At 4h, the greatest improvements in CGI-S and PANSS Total and Agitation scores were also seen in the 20-mg ziprasidone group. Responder rates (≥2 points decrease in BARS at 1.5h post-first-dose) were 80% in the 20-mg group (P=.006 vs 2 mg) and 58% in the 10-mg group; similar to the primary study. No dystonia or excessive sedation were reported in the 10- and 20-mg groups; 1 patient experienced akathisia in the 10-mg group.

Conclusion: Ziprasidone 10 and 20mg IM were rapidly effective and well tolerated in agitated psychotic patients with bipolar spectrum diagnoses, with the 20-mg IM dose producing the largest decrease in agitation.

Funding Source(s): Pfizer, Inc.

References:

NR781 Wednesday, May 5, 3:00 p.m.-5:00 p.m.
Switching From Noncholinergic Antidementia Treatment to Donepezil
Supported by Pfizer Inc. and Eisai
Alexander Kurz, M.D., Department of Psychiatry, Technical University Alzheimer Centre, Moehlstrasse 26, Munich 081675, Germany; Martin Kamleiter

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize that prior treatment of dementia with noncholinergic agents such as memantine does not impact upon the efficacy and safety of subsequent donepezil treatment in patients with mild to moderate Alzheimer's disease.

Summary:
Background: In Germany there is a history of using noncholinergic nootropic agents (including memantine) for the treatment of dementia.
Objective: To evaluate the efficacy and tolerability donepezil in patients with Alzheimer's disease (AD) who were switched from prior nootropic treatment.
Methods: 913 patients with mild to moderate AD were enrolled in Germany. The Mini-Mental State Examination (MMSE) evaluated cognition at baseline and after three months. Quality of life (QoL) was assessed on a three-point scale (improved/unchanged/worsened). Supportive data were obtained using the physician's global judgment of tolerability.
Results: Three cohorts were assessed: N- (n = 204; nootropic-naive patients), M+ (n = 112; memantine-pretreated patients), and N+ (n = 709; all nootropic-treated patients). All cohorts showed improvements in MMSE scores (N-, 2.51 ± 3.89; M+ 2.34 ± 3.84; N+ 2.12 ± 3.34) after three months. Improvements were comparable for QoL: 73.9% of patients improved in the N-cohort, 72.1% in M+, and 68.9% in N+. Investigators judged tolerability as very good or good in 93.1% of patients in the N-cohort, 95.5% in M+, and 95.2% in N+.
Conclusions: Switching from prior nootropic medications, including memantine, to donepezil therapy did not affect the efficacy of safety of donepezil.

Funding Source(s): Eisai GmbH and Pfizer GmbH, Germany

References:

NR782 Wednesday, May 5, 3:00 p.m.-5:00 p.m.
A Retrospective Comparative Study of Novel Antipsychotics in Major Depression
Adel A. Gabriel, M.D., Department of Psychiatry, Calgary University, 206 2723-37 Avenue NE, Calgary, AB T1Y5R8, Canada; Ian Forbes, M.D.

Educational Objectives:
Participants will have better awareness of the efficacy and tolerance of novel antipsychotics in psychotic mood disorders. Participants will be able to discuss critically recent literature pertaining to the use of novel-antipsychotics in major depression, with or without psychotic features.

Summary:
Background: The purpose of this study is to evaluate and compare the overall effectiveness of novel antipsychotics, quetiapine, olanzapine, and risperidone in the treatment of major depression with psychotic features. There are few controlled studies on olanzapine and risperidone, and no published literature on the effectiveness and tolerability of quetiapine in major depression.
Method: A retrospective study was carried out to identify charts of patients suffering from major depression with psychotic features, from both inpatients and outpatients of a teaching hospital, after ethical approval. Authors were able to identify 73 acute episodes with DSM-IV diagnosis of major depression with psychotic features (31 males, 42 females), with 28 patients on risperidone, 25 on quetiapine, and 20 on olanzapine, augmented treatments. Charts were reviewed for the clinical global impression changes, and tolerance to treatments over eight weeks.
Results: There was an overall significant clinical improvement in both the depressive and psychotic symptoms, which was supported by the significant changes in the severity subscale of the Clinical Global Impression scores ( CGI) in the three groups at eight weeks. However, there were no significant differences between the three treatment groups on the global improvement subscale scores at eight weeks of treatment, and the three antipsychotics were equally tolerated, and without significant extrapyramidal symptoms.
Conclusion: The evidence supports that there is an overall equivalent efficacy and tolerance in treating psychotic depression, with the three novel antipsychotics quetiapine, olanzapine or risperidone. Authors recommend that larger and prospective controlled trials will be necessary to examine the efficacy and long-term tolerance of the three novel anti-psychotics in major depression with or without psychotic features.

References:

NR783 Wednesday, May 5, 3:00 p.m.-5:00 p.m.
Olanzapine Versus Risperidone Treatment of Bipolar I Disorder
Supported by Eli Lilly and Company
Eileen B. Brown, Ph.D., Neuroscience, Eli Lilly and Company, 3880 Ridge Road, Nederland, CO 80466; Saeed Ahmed, M.D., Leslie M. Schuh, Ph.D., Robert W. Baker, M.D.

Educational Objectives:
At the conclusion of this session, participant should be able to discuss the effects of olanzapine and risperidone on global symptom severity during treatment of acute bipolar mania.

Summary:
Objective: In a direct comparison of patients with bipolar mania, olanzapine, and risperidone showed similar efficacy in mania ratings (Baker, APA 2003), but olanzapine had greater efficacy on clinician global impression of severity (CGI-S). This post-hoc analysis investigates possible determinants of this differential treatment effect.
**Method:** This three-week, double-blind study compared olanzapine (5–20 mg/day; N=165) with risperidone (1–6 mg/day; N=164) in manic or mixed episodes. Path analysis dissected the CGI-S treatment effect into drug effect explainable by effects on manic, depressive and extrapyramidal symptoms, measured by standard rating scales, versus other treatment effects not accounted for by rating scales.

**Results:** Olanzapine-treated patients achieved significantly greater improvement in CGI-S than risperidone-treated patients (p=.014). Approximately 93% of this effect was due to differences between olanzapine and risperidone (p=.006) not attributable to changes in mania or depression ratings or extrapyramidal symptoms. Race, gender, rapid cycling status, manic vs. mixed diagnosis, and weight change were not significant determinants of CGI-S change. Older olanzapine-treated patients had greater CGI improvement compared with older risperidone patients; no differences occurred between treatments for younger patients.

**Conclusions:** A significant drug effect not captured by standard rating scales was detected for olanzapine over risperidone on improvement of global illness severity.

**Funding Source:** Eli Lilly and Company

**References:**


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**NR784 Wednesday, May 5, 3:00 p.m.-5:00 p.m.**

**Effect of Olanzapine/Fluoxetine on Core Mood Symptoms in Bipolar Depression**

**Supported by Eli Lilly and Company**

Sara A. Corya, M.D., Lilly Research Labs, Lilly Corporate Center, Indianapolis, IN 46285; Susan D. Briggs, Ph.D., Michael Case, M.S., Mauricio F. Tohen, M.D.

**Educational Objectives:**

At the conclusion of this presentation, the participant should be able to explain the effect of olanzapine/fluoxetine combination on core mood symptoms in patients with bipolar I depression.

**Summary:**

**Background:** Depression scales frequently incorporate items addressing somatic symptoms such as disturbed sleep and appetite. Patients can experience improvements in these physical symptoms of depression while still having depressed mood. This post-hoc analysis examines the effect of olanzapine/fluoxetine combination on core mood symptoms in patients with bipolar I depression.

**Methods:** 833 subjects with bipolar depression were enrolled in this eight-week double-blind study and were randomized to olanzapine, placebo, or OFC. We analyzed a subset of 341 patients (olanzapine n=140; placebo n=138; OFC n=37) with significant anxiety symptoms (baseline HAM-A:18). Depression, anxiety, and treatment-emergent mania were evaluated using the MADRS, HAM-A, and YMRS, respectively.

**Results:** OFC (–13.2±11.8 SD) showed greater decreases in MADRS than placebo (–8.7±11.4 SD, p<.001 and p=.002, respectively). OFC had greater MADRS decreases than olanzapine (p=.04). OFC (–12.40±9.63 SD) and olanzapine (–7.98±8.83 SD) showed greater decreases in HAM-A than placebo (–6.13±8.34 SD, p<.001 and p=.044, respectively). OFC had greater MADRS decreases than olanzapine (p=.04). OFC (–16.5±10.4 SD) and olanzapine (–13.2±11.8 SD) showed greater decreases in MADRS than placebo (–8.7±11.4 SD, p<.001 and p=.002, respectively). OFC had greater MADRS decreases than olanzapine (p=.04). OFC (–12.40±9.63 SD) and olanzapine (–7.98±8.83 SD) showed greater decreases in HAM-A than placebo (–6.13±8.34 SD, p<.001 and p=.044, respectively). OFC had greater HAM-A decreases than olanzapine (p=.01). Treatment-emergent mania (baseline YMRS<15 and ≥15 post-baseline) was similar among groups (OF C 6.9%, olanzapine 8.6%, placebo 6.2%, p=.774).

**Conclusion:** OFC subjects experienced greater improvement in depression and anxiety symptoms than subjects on placebo or olanzapine without increased treatment-emergent mania.

**Funding Source(s):** Eli Lilly and Company

**References:**


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**NR785 Wednesday, May 5, 3:00 p.m.-5:00 p.m.**

**Olanzapine/Fluoxetine for Bipolar Depression With Comorbid Anxiety Symptoms**

**Supported by Eli Lilly and Company**

Sara A. Corya, M.D., Lilly Research Labs, Lilly Corporate Center, Indianapolis, IN 46285; Susan D. Briggs, Ph.D., Michael Case, M.S., Mauricio F. Tohen, M.D.

**Educational Objectives:**

At the conclusion of this presentation, the participant should be able to explain the effectiveness relative to placebo of olanzapine/fluoxetine combination (OFC) in bipolar I depressed patients with significant comorbid anxiety symptoms.

**Summary:**

**Background:** Occurring in approximately 30% of patients with bipolar disorder, anxiety has been associated with a greater likelihood of suicide attempts, alcohol abuse, resistance to lithium, and longer time to remission. This post-hoc analysis examines olanzapine/fluoxetine combination (OFC) in bipolar I depressed patients with comorbid anxiety.

**Methods:** 833 subjects with bipolar depression (baseline MADRS>20) were enrolled in this eight-week double-blind study and were randomized to olanzapine, placebo, or OFC. We analyzed a subset of 341 patients (olanzapine n=140; placebo n=138; OFC n=37) with significant anxiety symptoms (baseline HAM-A:18). Depression, anxiety, and treatment-emergent mania were evaluated using the MADRS, HAM-A, and YMRS, respectively.

**Results:** OFC (–10.4±7.4 SD) and olanzapine (–8.7±11.4 SD) showed greater decreases in MADRS than placebo (–6.2±7.6 SD, p<.001 and p=.02, respectively). Olanzapine/fluoxetine combination subjects also showed significantly greater improvement in the core mood index than olanzapine (p=.002).

**Conclusion:** Results suggest that MADRS improvement with olanzapine/fluoxetine combination represents core mood improvement and not just amelioration of the somatic symptoms of depression.

**Funding Source(s):** Eli Lilly and Company

**References:**


Elevated CSF Concentration of Substance P in Major Depression

Supported by Merck & Co., Inc.

Linda L. Carpenter, M.D., Department of Psychiatry, Butler Hospital/Brown University, 345 Blackstone Boulevard, Providence, RI 02908; Lawrence H. Price, M.D., Becky Kinkade, Ph.D., Tiesha Cassell, B.S., Gerard Sanacora, M.D., Michael J. Owens, Ph.D., Charles B. Nemeroff, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize neurobiological evidence regarding a potential role of substance P in major depression.

Summary:

Background: Recent drug development has focused on the substance P (SP)-preferring tachykinin receptor, neurokinin 1 (NK1). Results from preclinical and clinical investigations suggest that SP and the NK1 receptor are intimately linked with a diverse array of biological markers and neurotransmitter system abnormalities traditionally associated with mood and anxiety disorders. We hypothesized that lumbar CSF concentrations of SP would be elevated in medication-free depressed patients, relative to healthy controls.

Methods: Medication-free, adult outpatients with major depressive disorder (MDD, n=36) and healthy control subjects free of current or past psychiatric illness (CTR, n=49) underwent a single standard lumbar puncture at 12 noon. A total of 12 cc CSF was collected from the L3-L4 or L4-L5 interspace with a fine-gauge spinal needle. While symptom severity scores were not available for all depressed subjects, a minimum of 17 on the HAMD D scale was required for inclusion. Solid phase RIA assays were performed to determine CSF concentrations of SP.

Results: Depressed patients and healthy controls were similar in age and sex composition. CSF concentrations of SP were significantly higher among patients with MDD as compared with controls, after controlling for age effects (mean=75.7, SD=23.4 versus mean=51.7, SD=24; F=19.9, p<.0001).

Conclusion: This study of human CSF provides support for the notion that SP is a relevant neurotransmitter in the biology of major depression, and rationale for further investigation into the potential antidepressant utility of NK-1 receptor antagonists.

Funding Source(s): Procedures funded by a NARSAD Young Investigator Award (LLC) and a Brown University Pilot Project Award (LLC); Funding for assays (CBN, MJO) by Merck.

References:


Consistency of Patient-Reported Measures of Efficacy and Next-Day Function of Eszopiclone in Adults With Chronic Insomnia

Supported by Sepracor, Inc.

Milton K. Erman, M.D., Department of Psychiatry, Pacific Sleep Medicine Services, 10052 Mesa Ridge Court, #101, San Diego, CA 92121; Thomas Wessel, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to describe the daytime consequences of treatment with eszopiclone in patients with chronic insomnia.

Summary:

Objective: Fragmented sleep can affect next day function, yet daytime function is not typically evaluated in studies of hypnotics. Eszopiclone, a novel non-benzodiazepine under investigation to treat insomnia, has been shown to rapidly induce and maintain sleep.

Methods: Two long-term, randomized, double-blind, placebo-controlled studies of eszopiclone 3mg are presented. Both studies
included adults (age 21–64) with a DSM-IV definition of primary insomnia. Study A was a six-week study (n=204); Study B was a six-month study (N=788). Both studies captured patient reported sleep efficacy (onset, maintenance, quality) and next day function.

Results: Over the treatment period, eszopiclone significantly improved measures of sleep onset (p<0.0001), sleep maintenance (WASO, p<0.02), total sleep time (p<0.0001), and sleep quality (p<0.007) in both studies. These occurred in conjunction with improvements in daytime measures. In Study B, these measures were all statistically significant (p<0.0001), as well as sense of physical well-being (p<0.0001), which was not captured in Study A. In Study A, eszopiclone 3mg led to improvements in daytime alertness (p=0.059) and ability to function (p=0.12) vs. placebo.

Conclusions: Eszopiclone 3mg produced consistent efficacy in measures of sleep accompanied by improvements in daytime functioning, a novel finding in the study of hypnotics.

Funding Source(s): Sepracor Inc.

References:

NR790 Wednesday, May 5, 3:00 p.m.-5:00 p.m.
Diagnosing Bipolar Disorder in Research
Judith Jaeger, Ph.D., Cenorr Department, Zucker Hillside Hospital, 75-59 263rd Street, Glen Oaks, NY 11004; George Petrides, M.D., Rebecca Iannuzzo, Ph.D., Anil K. Malhotra, M.D., Donna O’Shea, Ph.D., Pam Derosse, M.A., Sherif Abdelmessih, B.A.

Educational Objectives:
At the conclusion of this session, the participant should recognize that diagnosing bipolar disorder in research endeavors may require more rigorous methods that are usually employed to avoid sample dilution.

Summary:
Objective: Diagnostic inclusion criteria for patients participating in research are often based on a psychiatrist’s clinical diagnosis (CD) or diagnosis from SCID interview with only minimal (or even without) historical case records. Reliability of these methods in bipolar disorders (BP) has not been investigated.

Method: We report on the relationship between CD and consensus SCID diagnosis in 81 cases. The latter was based on SCID interview, current/past inpatient records, and collateral interviews. All data collected were assembled into a SCID case review and presented at a diagnostic consensus conference. Expert senior faculty assigned lifetime Axis I diagnoses and diagnostic confidence ratings using a four point scale.

Results: 80.6% of patients having CD of BPI (86% BP spectrum) had equivalent consensus SCID. Confidence for those cases where there was agreement between CD and SCID for BPI or BP spectrum was significantly higher than cases where CD/SCID did not agree.

Conclusion: The finding that approximately one out of every five recruits to a BP study proved not to meet criteria for the target disease should raise concern among BP researchers as treatment effectiveness studies targeting bipolar disorder may be subject to considerable sample dilution when less rigorous methods are used.

Funding Source(s): NIMH Funded: RO1MH60904-0

References:

NR789 Wednesday, May 5, 3:00 p.m.-5:00 p.m.
Higher OCD Comorbidity in Bipolar Than Unipolar Patients
Suhayl J. Nasr, M.D., NASR Psychiatric Services PC, 2814 South Franklin Street, Michigan City, IN 46360-1843; Burdette Wendt

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize that OCD comorbidity is more frequent in bipolar patients than unipolar patients.

Summary:
Objective: To examine the frequency of certain comorbid illnesses in bipolar compared to unipolar outpatients.

Methods: The Mini Structured Clinical Interview for Diagnosis (MiniSCID) and the Symptom Checklist90 (SCL90) were administered to all outpatients 18 to 65 years old. The following data report on all current patients whose last name starts with A to H.

Results: 257 patients completed the MiniSCID. There were 87 Bipolar and 170 Nonbipolar patients. Bipolar patients had an average of 8.8 other diagnoses compared to 7.2 in nonbipolar patients (p<0.001). There was a significantly higher comorbidity of obsessive-compulsive disorder in the bipolar patients (62% Vs 36%, p=0.00006). The frequency of panic disorder (57% Vs 47%) and social anxiety disorder (56% Vs 60%) was similar in both groups. 340 patients completed the SC190. There were 113 bipolar and 227 nonbipolar patients. All subscales showed significantly elevated scores in the bipolar patients (p<0.001 or more). Obsession/compulsion, depression and hostility were the most significantly elevated scores.

Conclusions: Comorbidity is the rule in bipolar disorder as measured by the MiniSCID. OCD is more often seen in bipolar than unipolar patients.

Funding Source(s): None other than my practice.

References:

NR791 Wednesday, May 5, 3:00 p.m.-5:00 p.m.
Outpatient Treatment: A Pragmatic RCT With Three Types of Psychotherapy
Annemieke Van Straten, Ph.D., BMG, Erasmus Medical Center, PO Box 1736, Rotterdam 3000 DR, Netherlands; Bea Tiemens, Ph.D., Leona Hakkaart, Ph.D., Marianne C. Donker, Ph.D.
Educational Objectives:
At the conclusion of this session, the participant should be able to realize that patients with mood or anxiety disorders will not be harmed if they are initially offered a very short form of psychotherapy, provided within a stepwise mode of service provision.

Summary:
Objective: It is still unknown which of the numerous psychological treatments is most cost-effective for patients with mood and/or anxiety disorders. In this study we compared the effectiveness of cognitive behavioral therapy (CBT), brief solution focused therapy (SFT), and care as usual (CAU). In CAU a specific form of psychotherapy is chosen from a broad range of therapeutic orientations for each individual patient.

Method: a pragmatic RCT was carried out in daily practice of 8 Dutch outpatient mental health care centers, and included 702 patients. All patients were interviewed at home one year and one and a half to two years after baseline to reassess the DSMIV diagnoses with the CIDI.

Results: At baseline 12% of all patients suffered an anxiety disorder, 47% a mood disorder, while the remaining 41% suffered both. One year thereafter, 51% of the patients were diagnosed free and at the end of the study 66% was diagnoses free. However, there were no statistically significant differences in effectiveness between the three treatment conditions.

Conclusions: There is no indication that care as usual is more effective than a stepped care approach where either CBT or BT is offered as the first treatment.

Funding Source(s): Netherlands Organization for Health Research and Development (ZonMw) and SBWOGG

References:

NR792 Wednesday, May 5, 3:00 p.m.-5:00 p.m.
Brain MRI, White-Matter Lesions, and Major Depression With Anger Attacks
Dan V. losifescu, M.D., Department of Psychiatry, Massachusetts General Hospital, 50 Staniford Street, #401, Boston, MA 02114; Perry F. Renshaw, M.D., In Kyoon Lyoo, M.D., Ho Kyo Lee, M.D., Roy H. Perlis, M.D., Bettina Bankier, M.D., Maurizio Fava, M.D.

Educational Objectives:
- At the conclusion of this session, the participant should be able to recognize the association between brain MRI white matter hyperintensities ("vascular depression") and major depressive disorder with anger attacks.

Summary:
Objective: To investigate the relationship of MRI-defined brain white matter hyperintensities (WMH) with clinical subtypes of major depressive disorder (MDD) in non-elderly subjects.

Method: 68 subjects (mean age 40.1 ± 9.8 years; 41% female) meeting DSM-III-R criteria for major depressive disorder and 35 matched normal controls were administered brain magnetic resonance imaging (MRI) scans at 1.5T to detect T2 white matter hyperintensities. We used the Fazekas scale (Fazekas et al, 1987) to generate severity scores (range 0-3) for total WMH, periventricular WMH, and subcortical WMH. We assessed clinical subtypes of depression: melancholic depression (DSM-IV criteria); atypical depression (Atypical Depression Diagnostic Scale; Stewart et al, 1992); depression with anger attacks (Anger Attacks Questionnaire; Fava et al. 1991). We used logistic regression to assess associations between depressive subtypes and white matter lesions severity scores, adjusting for age and gender.

Results: The incidence and severity of brain white matter hyperintensities was not statistically different between MDD subjects and healthy volunteers (p > 0.05). Major depression with anger attacks was associated with higher severity of total white matter hyperintensities (p < 0.02), and with higher severity of subcortical WMH (p < 0.04), but not with periventricular WMH (p > 0.05). Atypical and melancholic MDD subtypes were not significantly associated with any of the brain WMH severity scores (p > 0.05 for all analyses).

Conclusion: Major depressive disorder with anger attacks is associated with higher incidence of brain white matter lesions, especially in the subcortical areas. Our finding is consistent with previous studies which have shown an association between anger and vascular disease.

Funding Source(s): NARSAD Young Investigator Award (Dr. losifescu), NIMH grant R01-MH48483 (Dr. Fava)

References:

NR793 Wednesday, May 5, 3:00 p.m.-5:00 p.m.
In Early Adolescence, Do Levels of Physical Activity Predict Depression?
Supported by GlaxoSmithKline
Gunnar Morken, M.D., Department of Neuroscience, NTNU, Box 3008 Lade, Trondheim 7043, Norway; Anne Marie Sund, M.D.

Educational Objectives:
- At the conclusion of this session, the participant should recognize low levels of physical activity as a risk factor for depression among young adolescents.

Summary:
Introduction: In early adolescence do levels of physical activity predict levels of depressive symptoms scores one year later?
Methods: 12-15 year adolescents (N=2465) answered questionnaires twice with one year apart during the years 1998 to 1999. The Mood and Feelings Questionnaire (MFQ) is a 34-items questionnaire covering affective, melancholic, vegetative, cognitive and suicidal aspects of depression. The number of hours spent on vigorous exercise, on non-vigorous physical activities and sedentary activities were registered.

Results: Boys reported more time spent on vigorous exercise than girls, [(t2217)=−9.8, p<0.001]. The mean number of reported stressful events for the previous year was 4.5 (SD=3.7) for the whole sample and no significant sex difference was found. Analyzing high scorers of depressive symptoms at Time Two in a hierarchical logistic regression analysis showed that both high levels of sedentary activities and a low levels of vigorous exercise at Time One predicted significantly the odds for being a high scorer (MFQ≥26) at Time Two.

Conclusions: Low levels of vigorous exercise and high levels of sedentary activities constitute independent risk factors for develop-
opining depressive symptoms in a one-year perspective among young adolescents.

**Funding Source(s):** Glaxo Smith Kline (travel expenses)

**References:**


**NR794 Wednesday, May 5, 3:00 p.m.-5:00 p.m.**

**Patient Substance/Alcohol Abuse and Caregiver Burden in Bipolar Disorder**

Michael J. Ostacher, M.D., Department of Psychiatry, Massachusetts General Hospital, 50 Staniford Street, Suite 580, Boston, MA 02114; Robert A. Rosenheck, M.D., Nancy Wolff, Ph.D., Deborah A. Perlick, Ph.D., David Miklowitz, Ph.D., Polina Eidelman, B.A., Joseph R. Calabrese, M.D., Mark D. Fossey, M.D., Jodi Gonzalez, Ph.D., Terence A. Ketter, M.D., Lauren B. Marangell, M.D., Jayendra K. Patel, M.D., Terence Ketter, M.D., Lauren B. Marangell, Jayendra Patel, M.D., Nancy Wolff, Ph.D., Robert Rosenheck, M.D.

**Educational Objectives:**

At the conclusion of this session, the participant should be able to recognize the impact of comorbid substance or alcohol abuse in bipolar patients on the health of their caregivers.

**Summary:**

**Objective:** This study evaluated well-being in caregivers of bipolar patients with comorbid alcohol or substance abuse enrolled in a naturalistic study of bipolar disorder, the Systematic Treatment Enhancement Program for Bipolar Disorder.

**Method:** 142 caregivers were interviewed at study admission on measures of burden, health behaviors, and coping. Patients' substance and alcohol abuse were assessed by semi-structured interview at medication management visits within four weeks of the caregiver interviews.

**Results:** 6.3% of patients were identified as currently abusing alcohol and 3.5% as abusing substances. Patient substance abuse was associated with more use of health services (t = -4.70, p<0.001), riskier health behaviors (t = -2.16, p = 0.05), lacking time to exercise (t = -2.55, p < 0.05), and delaying medical care (t = -2.29, p < 0.05) in caregivers. There was a trend toward higher depression scores (t = -1.77, p < 0.10) and using substances more often to cope (t = -1.95, p < 0.10) in these caregivers. Patient alcohol abuse was associated with caregivers using more health services (t = -2.16, p < 0.05), practicing riskier health behaviors (t = -2.27, p < 0.05), lacking time to exercise (t = -2.71, p < 0.01), delaying medical care (t = -2.23, p < 0.05), and canceling doctor's appointments (t = -2.11, p < 0.05). The level of overall burden for these caregivers was not increased.

**Conclusions:** Comorbid substance or alcohol abuse in bipolar patients is associated with increased health service use and added health risk for their caregivers, although overall burden is not increased.

**Funding Source(s):** National Institute of Mental Health

**References:**


**NR795 Wednesday, May 5, 3:00 p.m.-5:00 p.m.**

**Efficacy of Aripiprazole Versus Placebo in Acute Mania: Pooled Analysis**

Supported by Bristol-Meyers-Squibb and Otsuka Pharmaceutical Co., Ltd.

Robert D. McQuade, Ph.D., Bristol-Myers Squibb Company, Route 206 & Province Line Road, Princeton, NJ 08543; Raymond Sanchez, M.D., William H. Carson, Jr., M.D., Susan Kostic, Ph.D., Neveen Abon-Gharbia, Pharm.D., Taro Iwamoto, Ph.D., Sterling A. Hardy, Ph.D.

**Educational Objectives:**

At the conclusion of this presentation, the participant should be able to better understand the efficacy of aripiprazole for treatment of acute manic episodes in patients with bipolar I disorder.

**Summary:**

**Objective:** Demonstrate the efficacy of aripiprazole in the treatment of acute mania in patients with bipolar disorder.

**Methods:** Data were pooled from three three-week, double-blind, multicenter studies in 899 patients with acute mania randomized to aripiprazole (n=515) or placebo (n=384). The key outcome measures included change from baseline in the Young Mania Rating Scale (Y-MRS) Total Score, response rate (based on ≥50% decreases in Y-MRS) and remission rate (based on Y-MRS-Total Score ≤12).

**Results:** Treatment with aripiprazole led to significantly greater Y-MRS Total Score reduction, response rate, and remission rate compared with placebo, as early as Day 4 and maintained throughout the study. Y-MRS Total Score reduction for aripiprazole vs placebo was -6.63 vs -4.59 (p<0.001) at Day 4 and continued to improve over the 3 weeks to study endpoint (-10.08 vs -6.87, p<0.001). As compared with placebo, more improvement was seen on all of the individual Y-MRS items with aripiprazole. Significantly more patients responded with aripiprazole compared with placebo (45% vs 30%, p<0.001) and significantly more patients attained remission by study endpoint (42% vs 28%, p<0.001).

**Conclusion:** Aripiprazole is effective in treating symptoms of acute mania.

**Funding Source(s):** Bristol-Myers Squibb Company and Otsuka Pharmaceutical Co., Ltd.

**References:**


The majority of these adverse events were mild to moderate and prazole is an important addition in the armamentarium for acute prolongation, and somnolence, suggests that aripiprazole elevation, QT\(C\) excluded headache, nausea, dyspepsia, agitation, and akathisia.

Results: Discontinuations due to adverse events were similar between aripiprazole and placebo (11% vs 10%). More common adverse events reported in ≥15% of patients on aripiprazole included headache, nausea, dyspepsia, agitation, and akathisia.

Conclusion: The favorable safety and tolerability profile of aripiprazole, including low potential for EPS, weight gain, prolactin elevation, QT\(C\) prolongation, and somnolence, suggests that aripiprazole is an important addition in the armamentarium for acute mania.

Funding Source(s): Bristol-Myers Squibb Company and Otsuka Pharmaceutical Co., Ltd.

References:


Objectives: To evaluate the 23-year follow-up personal resources, life contexts, and health outcomes associated with nonremission in a cohort of patients treated for unipolar depression.

Method: In 1980 and 1981, 424 patients treated for unipolar depression were assessed on their personal resources, life contexts, psychological and physical well-being, and role functioning. Of the surviving baseline cohort, 73% participated 23 years later. Consistently nonremitted (18%) and partially remitted/remitted (82%) groups were identified using DSM-IV depressive symptoms at 10 years and 23 years after index treatment.

Results: Compared with remitted patients, nonremitted patients showed poorer physical, psychological, and social functioning. Nonremitted patients reported more medical symptoms (6.37 vs. 3.35; \(p<.001\)) and conditions (2.57 vs. 1.27; \(p<.001\)) than remitted patients who were more easy-going (20.20 vs. 16.66; \(p<.001\)), less anxious (1.15 vs. 2.60; \(p<.001\)) and had higher self-concept (12.54 vs. 8.57; \(p<.001\)). Nonremitted patients also earned less income ($20,200 vs. $36,025; \(p<.018\)) and were unemployed for more months during the past year (4.93 vs. 1.74; \(p<.001\)). Nonremitted patients had fewer and poorer quality social resources (12.73 vs. 16.16; \(p<.001\)) and used more avoidance coping (6.46 vs. 3.99; \(p<.001\)).

Conclusion: After controlling for socio-demographics, treated patients who were still depressed 10 and 23 years after an initial depressive episode show worse psychological, physical, and occupational functioning and poorer social and personal resources than remitted patients.

Funding Source(s): Eli Lilly and the Department of Veterans Affairs Health Services Research and Development Service.

References:


Objectives: To illustrate the extent of the long-term burden of nonremitted depression on health outcomes, as well as on occupational functioning and personal and social resources.

Method: MOD patients (18–65 years) who were partial and non-responders to an adequate course of SSRI monotherapy (≥ 8 weeks) and on a stable SSRI dose (≥ 4 weeks) who had a screening/baseline 31-item Hamilton Depression Scale (HAMD-31) score of 14–26 (inclusive), Epiworth Sleepiness Scale (ESS) score
Patients were randomized to modafinil 200 mg/day or placebo for eight weeks. Assessments included the Global Impression of Change (CGI-C), HAMD-D-31, HAMD-D-17, FSS, and Brief Fatigue Inventory (BFI).

Results: Of N=311 randomized, 135 modafinil-treated and 130 placebo-treated patients completed. Significantly higher rates of improvement on the CGI-C were found at endpoint (85% modafinil vs 53% placebo; p<.05). There was a trend toward greater mean reductions in HAMD-D-31, HAMD-D-17, and FSS at endpoint (modafinil vs placebo, p<.08). At endpoint, modafinil significantly reduced mean BFI (worst) scores (p<.05 vs placebo); no significant differences were found in FSS and BFI. The most commonly reported adverse events were headache (13% modafinil; 16% placebo), nausea (9%; 2%), dizziness (7%; 2%), and dry mouth (6%; 3%).

Conclusions: This study suggests that modafinil is a safe and effective augmenting agent for partial and non-response to SSRI treatment in MDD.

Funding Source(s): Supported by Janssen Research and Development, LLC.

References:

NR800 Wednesday, May 5, 3:00 p.m.-5:00 p.m.
Predictors of Time to Relapse in Bipolar I Disorder Supported by Eli Lilly and Company
Mauricio F. Tohen, M.D., Department of Research, Eli Lilly and Company, One Lilly Corporate Center, Indianapolis, IN 46285; Charles L. Bowden, M.D., Joseph R. Calabrese, M.D., Gary S. Sachs, M.D., Richard Riser, M.S., Holland C. Delke, Ph.D., Hua-Qiong Shen, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to discuss the clinical predictors of time to bipolar relapse.

Summary:
Background: In bipolar disorder, optimal treatment planning depends upon early prediction of illness course.1,2 The following post-hoc analyses examined predictors of time to relapse using pooled data from two bipolar maintenance studies.

Methods: Subjects were 779 patients who achieved symptomatic remission from a manic or mixed index episode and entered double-blind maintenance therapy for up to 48 weeks with olanzapine (n=434), lithium (n=213), or placebo (n=132) following 6–12 weeks of acute open-label treatment with either olanzapine (Study 1) or olanzapine-lithium cotherapy (Study 2). Various patient and illness characteristics were assessed as possible predictors using Cox regression analyses, adjusted for therapy.

Results: Rapid cycling course, mixed index episode, number of mood episodes in the past year, early onset, bipolar family history, female gender, and lack of prior hospitalization for bipolar disorder were all significant predictors of shorter time to relapse. Stepwise analysis suggested that history of rapid cycling and a mixed index episode were the strongest predictors of time to relapse. Analysis by type of maintenance therapy also yielded differential predictors.

Conclusions: These results from ARISe-RD, the largest trial of atypical antipsychotic augmentation in resistant depression, indicate that low-dose risperidone augmentation may provide safe, rapid, and robust improvement in depressive symptoms and associated anxiety. Positive results from the relapse prevention phase would suggest a role for risperidone augmentation for maintenance treatment in resistant depression.

Funding Source(s): Supported by Janssen Research and Development, LLC.

References:
NR801  Wednesday, May 5, 3:00 p.m.-5:00 p.m.

Predictors of Response to Olanzapine and Fluoxetine in Bipolar Depression
Supported by Eli Lilly and Company

Mauricio F. Tohen, M.D., Department of Research, Eli Lilly and Company, One Lilly Corporate Center, Indianapolis, IN 46285; Eduard Vieta, M.D., Joseph R. Calabrese, M.D., Terence A. Ketter, M.D., Philip Mitchell, M.D., Susan D. Briggs, Ph.D., Michael Case, M.S.

Educational Objectives:
At the conclusion of this session, the participant should be able to discuss the clinical predictors of response to olanzapine and olanzapine/fluoxetine combination in patients with bipolar depression.

Summary:
Background: Both olanzapine/fluoxetine combination (OFC) and olanzapine monotherapy have shown effectiveness in bipolar depression relative to placebo; however, the patient variables that predict response to olanzapine versus olanzapine/fluoxetine combination are unknown. The purpose of this analysis was to identify predictors of response to either olanzapine or OFC in bipolar depression.

Methods: Stepwise logistic regression was performed on acute phase data from a double-blind, randomized clinical trial comparing olanzapine, OFC, and placebo for bipolar I depression. Regressions were run separately for olanzapine, OFC, and placebo subjects. Response was defined as ≥50% decrease in MADRS total score at endpoint.

Results: A set of four variables was significant for predicting response to olanzapine: race, absence of rapid cycling, duration of current episode, and number of manic episodes in the past 12 months (model χ²=30.18, p<.001). One independent variable was significant for predicting response to OFC: onset of bipolar disorder before age 20 (model χ²=4.47, p=.035). Four variables were significant for predicting response to placebo: race, body mass index, absence of melancholic features, and family history of bipolar disorder (model χ²=21.29, p<.001).

Conclusion: Response in a sample of bipolar depressed patients was predicted by different profiles of patient characteristics for olanzapine, OFC, and placebo.

Funding Source(s): Eli Lilly and Company

References:

NR803  Wednesday, May 5, 3:00 p.m.-5:00 p.m.

The Cost-Effectiveness of Brief Verbal Therapy

Leona Haakkaart, Ph.D., Erasmusmc, IMTA, PO Box 1738, Rotterdam 3000DR, Netherlands; Annemieke Van Straten, Ph.D., Bea Tiemens, Ph.D., Marianne C. Donker, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to realize that assessment of the costs should be done preferably from a societal perspective because savings within the mental health care center may be compensated by costs increases in other parts of the health care or society.

Summary:
Introduction: Due to waiting lists and cost control, Brief Verbal Treatment (BT) has achieved popularity. The (cost-)effectiveness of BT compared to cognitive-behavior therapy (CBT) and care as usual (CAU) is unknown. This study assessed the cost-effectiveness of BT compared with CBT and CAU for patients with depressive and anxiety disorders.

Methods: A pragmatic RCT was carried out in eight Dutch mental health care centers (MHC), and included 702 patients. Patients were interviewed at baseline and then every three months over a period of 1.5 years. Detailed data on medical health care utilization (direct costs) and production losses due to absence from work (indirect costs) as well as quality of life was collected every three months.

Results: The direct costs for treatment at the MHC were significantly lower for BT. However, the overall costs were not significantly different. The quality of life score improved over time with no significant difference between the groups.

Conclusion/discussion: BT is a cost-effective treatment for the MHC, however from a societal perspective (including all costs) there was no difference in cost-effectiveness between the three treatments.
Lamotrigine Improves Mood in Patients With Epilepsy
Supported by GlaxoSmithKline
Robert P. Kustra, Pharm.D., GlaxoSmithKline, 3030 Cornwallis Road, Research Triangle, NC 27709; Chris Sackellares, M.D., Anne E. Hammer, B.S., John A. Messenheimer, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the effect of lamotrigine on mood in patients with epilepsy.

Summary:
Rationale: Lamotrigine (LTG) has been shown effective in maintenance treatment of bipolar disorder. Additional studies have shown positive mood effects of LTG in patients with epilepsy. This study evaluated the effect of LTG on mood in patients with epilepsy.

Methods: Data for this analysis were collected as part of a large outpatient study. Patients aged 16 years and older entered the study either because they required a change in their current antiepileptic drug (AED) therapy. Open-label LTG was titrated according to labeling to a target dose of 300-500 mg/day (100-400 mg/day for patients on an AED regimen containing valproate), continued for sixteen weeks. Patients on a single enzyme-inducing AED were eligible to convert to LTG monotherapy for an additional twelve weeks. Mood was assessed with the profile of mood states (POMS) at baseline and at the end of both the adjunctive and monotherapy phases.

Results: 196 patients enrolled (mean age 43 years, 58% female). At baseline, the majority of patients were taking carbamazepine (43%), phenytoin (34%), or valproate (19%). Of the 196 patients, 152 (78%) completed the adjunctive phase. Of the 68 patients converting to monotherapy, 56 (82%) completed. Mean POMS total mood disturbance improved from 54 at baseline to 33 at endpoint. Consistent with previous work, the correlation between Q-LES-Q and MADRS total change scores at endpoint was 0.6.

Conclusions: These findings suggest that augmentation with risperidone rapidly and significantly improves quality of life in TRD patients. Consistent with previous work, the correlation between Q-LES-Q and MADRS total change scores was observed as early as day 7 (P < 0.0001). Q-LES-Q item 15, medication satisfaction, was rated as good or very good by 61% of subjects. Correlation between Q-LES-Q and MADRS total change scores at endpoint was 0.6.

References:

NR805 Wednesday, May 5, 3:00 p.m.-5:00 p.m.
Improvement in Quality of Life With Risperidone Augmentation in Treatment-Resistant Depression Supported by Janssen Pharmaceutica and Research Foundation
David Walling, Ph.D., CNS Network, 12772 Valley View Street, Garden Grove, CA 92845; Marcia Rupnow, Ph.D., Carla M. Canuso, M.D., Georges Gharabawi, M.D., Ibrahim Turkoz, M.S., Mark H. Rapaport, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to describe the improvements in quality of life and symptom relief after treatment with risperidone augmentation in patients with treatment-resistant depression.

Summary:
Objective: To evaluate the effect of adjunctive risperidone treatment on quality of life in patients with treatment-resistant depression (TRD).

Methods: Data from the open-label treatment phase (4-6 weeks) of an international study designed to evaluate the efficacy, safety, and maintenance effect of risperidone augmentation to SSRI treatment in TRD. Quality of life was evaluated using the short form of Quality-of-Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q). Change in Q-LES-Q from baseline was analyzed by paired t test. Correlation analyses between MADRS and Q-LES-Q change scores were performed using Pearson method.

Results: This analysis included 386 subjects, mean age 47.1. Baseline and endpoint mean (SD) Q-LES-Q scores were 42.8 (14.6) and 56.0 (18.6), indicating an improvement of 13.2 with risperidone augmentation (P < 0.0001). Significant improvements were observed within as early as day 7 (P < 0.0001). Q-LES-Q item 15, medication satisfaction, was rated as good or very good by 61% of subjects.

Conclusions: These findings suggest that augmentation with risperidone rapidly and significantly improves quality of life in TRD patients. Consistent with previous work, the correlation between Q-LES-Q and MADRS indicates a meaningful relationship between quality of life improvement and symptom relief.

References:
functioning in patients with bipolar disorder experiencing manic or mixed episodes.

Summary:

**Objective:** To understand risperidone’s effect on functioning in bipolar patients.

**Methods:** Post-hoc analysis of Global Assessment Scale (GAS) scores from two randomized, placebo-controlled, three-week trials of risperidone in patients with bipolar I disorder, currently manic (US and ex-US studies) or mixed (ex-US study). GAS scores from 1–100, were examined on a categorical basis (10 point/category increments) using LOCF (endpoint) and completer analyses. Between-group analyses used Cochran-Mantel-Haenszel test, controlling for site and psychotic symptoms at baseline.

**Results:** Baseline GAS scores were comparable between risperidone and placebo, with 89% to 96% of patients scoring below 50, indicating serious symptoms and/or impairment in social or occupational functioning. At endpoint, significantly more risperidone-treated patients, 52.4%-US; 78.3%-ex US, scored >50 vs placebo 27.7%-US; 41.5%-ex US (p<0.001; p<0.001). Among study completers, 76.8% (US) and 84.6% (ex-US) of risperidone-treated patients scored >50 (p<0.05 and p<0.001 vs placebo). From baseline, 42.9% (US) and 75.5% (ex-US) of risperidone-treated patients improved by ≥2 GAS categories (p=0.001; p=0.001 vs placebo). Among completers, ≥2 category improvement rates were 35% and 32% for venlafaxine XR and SSRIs, respectively (P=NS). Mean maximum prescribed doses were venlafaxine XR 157 mg/day, fluoxetine 55 mg/day, paroxetine 41 mg/day, citalopram 35 mg/day, and sertraline 135 mg/day.

**Conclusions:** These results suggest that venlafaxine XR is an effective treatment for MDD, and may bring patients to remission earlier in treatment compared with SSRIs when treatment algorithms and guidelines for duration of therapy are used.

**Funding Source:** Wyeth Research

References:


**NR807 Wednesday, May 5, 3:00 p.m.-5:00 p.m.**

**Treatment Algorithms in Depression: Remission With Venlafaxine Extended Release Versus SSRIs Supported by Wyeth Pharmaceuticals**

Isma Benattia, M.D., Wyeth Research, 500 Arcola Road, Collegeville, PA 19426; Jeff Musgnugn, Jay Graepel, Ph.D.

**Educational Objectives:**

At the conclusion of this session, the participant will learn the remission rates in patients treated for depression in current primary and psychiatric care. Remission rates will be correlated with functional impairment, socio-economic factors, and type of treatment.

**Summary:**

**Objective:** Treatment of depression should result in absence of symptoms, i.e., remission, to restore the functional state of the patient and reduce the risk of relapse. OREON aims to determine remission rates in patients treated for depression in primary care. Remission rates will be correlated with functional status, type of treatment and socio-economic factors.

**Methods:** In this open-label, rater-blind, multicenter study, patients treated with venlafaxine XR or SSRIs using treatment algorithms and length of treatment guidelines.

**Results:** 300 GP’s and 60 psychiatrists are screening 3600 patients. Partial results indicate low remission rates in patients treated for depression. Absence of remission is associated with higher disability. Data are analyzed to assess whether type of treatment and socio-economic factors impact on remission rates.

**Final report is planned for March 15.**

**Conclusions:** OREON is the first study to show remission rates in patients treated for depression in a naturalistic setting. Many patients present important levels of residual symptoms.

**Funding Source:** Wyeth Pharmaceuticals Belgium

References:

NR809  Wednesday, May 5, 3:00 p.m.-5:00 p.m.
SSRI Utilization Patterns and the Economic Consequences of Early Discontinuation
Supported by GlaxoSmithKline
Michael Eaddy, Pharm.D., Applied Health Outcomes, 3488 East Lake Road, Suite 201, Palm Harbor, FL 34685; David V. Sheehan, M.D., Tim Regan, R.Ph., Matt Sarnes, Pharm.D.

Educational Objectives:
(1) To describe current treatment patterns associated with depression management; (2) To describe the economic consequences of current utilization patterns in a managed care setting; (3) To recognize the ongoing challenges in managing depression and the need for continuous quality improvement in this condition

Summary:

Introduction: Thompson et al showed that, in the early 1990s, depression patients remaining on SSRI therapy for at least 90 days incurred lower medical costs than patients who did not. The purpose of this study was to re-evaluate the economic consequences of various SSRI utilization patterns in today’s healthcare environment.

Methods: Patients receiving two or more SSRI prescriptions between 01/01/01 and 12/31/02 were eligible for study inclusion. Patients were required to have continuous eligibility six months prior and 12 months after their index date and no psychosis-related or substance abuse disorders or medications. Patients were placed into antidepressant utilization cohorts (1) < 90 days, (2) 90–179 days, (3) >180 days, (4) >90 days with titration, (5) partially compliant (PC), and (6) therapy change (TC). Annual medical and depression-related pharmacy costs were then compared.

Results: There were 65,753 patients included in the study. Total annual healthcare costs (medical + depression-related pharmacy costs) were lowest in the 90–179 cohort, ($5,141); compared with >180 ($6,202), <90 ($6,797), PC ($6,711), titration ($7,442), and TC ($9,030) cohorts.

Conclusions: Fully compliant patients remaining on therapy for longer than 90 days without evidence of titration or therapy change incurred the lowest annual healthcare costs. Patients with evidence of therapy change incurred the highest costs.

Funded by GlaxoSmithKline

References:

NR810  Wednesday, May 5, 3:00 p.m.-5:00 p.m.
Effectiveness of Atypical Antipsychotics in Nonpsychotic Unipolar Depression
Supported by Janssen Pharmaceuticals and Research Foundation
Ron P. Welch, B.Sc., Psychiatry Department, Alberta Hospital Edmonton, Box 307, Edmonton, AB T5J 2J7, Canada; Mark H. Snaterse, B.Sc., John C. Lind, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to better understand the efficacy of aripiprazole in bipolar disorder patients with acute mixed episodes, rapid cycling, and greater severity of symptoms.

NR811  Wednesday, May 5, 3:00 p.m.-5:00 p.m.
Efficacy of Aripiprazole in Subpopulations of Bipolar Disorder
Supported by Bristol-Meyers-Squibb and Otsuka Pharmaceutical Co., Ltd
Darlene Jody, M.D., Bristol-Meyers Squibb Company, Route 206 and Province Line Road, Lawrenceville, NJ 08643-4000; Robert D. McQuade, Ph.D., William H. Carson, Jr., M.D., Taro Iwamoto, Ph.D., Neveen Abou-Gharbia, Pharm.D., Sterling A. Hardy, Ph.D., Donald G. Archibald, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the utility of the atypical antipsychotics in the treatment of non-psychotic unipolar depression and to demonstrate an understanding of the cost effectiveness of the various agents.

Summary:

Objectives: To investigate the patterns of utilization of the three most commonly prescribed atypical antipsychotics in a large Canadian psychiatric hospital in order to determine and compare health outcomes and cost effectiveness.

Methods: Medical records were reviewed for patients admitted from October 2000 to September 2003 with a DSM-IV diagnosis of major depressive disorder. Means were calculated for length of admission, re-hospitalization rates, Global Assessment of Functioning (GAF), Clinical Global Impression Scores (CGI), and pharmacoeconomic variables. There were no significant between group differences in age, years of illness, number of admissions, gender, history of drug abuse, history of suicide, marital status, antidepressant exposure, and level of education.

Results: A total of 131 patients qualified for the study (olanzapine = 58; risperidone = 37; quetiapine = 36). Mean CGI and GAF on admission, discharge and overall improvement were similar for all cohorts. The mean cost/day was olanzapine $5.79, quetiapine $3.00, risperidone $2.18. The six-month re-hospitalization rates were 40% for olanzapine, 22% for quetiapine and 21% for risperidone.

Conclusions: Atypical antipsychotics were chosen for patients with moderate to severe illness. Our results indicate similar overall effectiveness during the acute/inpatient phase for each of the three agents. A total of 131 patients qualified for the study (olanzapine = 58; risperidone = 37; quetiapine = 36). Mean CGI and GAF on admission, discharge and overall improvement were similar for all cohorts. The mean cost/day was olanzapine $5.79, quetiapine $3.00, risperidone $2.18. The six-month re-hospitalization rates were 40% for olanzapine, 22% for quetiapine and 21% for risperidone.

Support provided by Janssen Pharmaceutical Canada

References:
Summary:

Objective: Demonstrate efficacy of aripiprazole in bipolar disorder patients with acute mixed episodes, rapid cycling, and those with greater severity of symptoms.

Methods: In three three-week, double-blind, multicenter studies, 899 patients with acute mania were randomized to aripiprazole (n=515) or placebo (n=384). The main outcome measure was change from baseline in Young Mania Rating Scale (YMRS). The data from the three trials were pooled and patient population was stratified according to characteristics of the episode (manic vs mixed), disease history (rapid cycling), and symptom severity.

Results: In patients with acute mixed episodes, treatment with aripiprazole resulted in significant reductions in YMRS compared with placebo (−9.7 vs −7.4, p=0.044), similar to those observed for patients with manic episodes (−10.4 vs −6.5, p<0.001). In patients with rapid cycling bipolar disorder, significant reductions in YMRS occurred with aripiprazole vs placebo (−10.6 vs −5.5, p=0.001). In patients presenting with more severe symptoms (YMRS >27), treatment with aripiprazole resulted in greater improvement vs placebo (−11.6 vs −6.8, p<0.001). Aripiprazole was also equally efficacious in patients with or without psychotic symptoms.

Conclusion: For the treatment of bipolar disorder, aripiprazole consistently resulted in significant improvement in patients with manic or mixed episodes, rapid-cycling bipolar disorder, and in patients with or without psychotic symptoms.

Funding Source(s): Eli Lilly and Company

References:

NR812 Wednesday, May 5, 3:00 p.m.-5:00 p.m. Improved Cognitive Outcome With Olanzapine Treatment in Bipolar Patients Supported by Eli Lilly and Company

Deborah A. Yurgelun-Todd, Ph.D., Department of Neuroimaging, McLean Hospital, 115 Mill Street, Belmont, MA 02478; Staci A. Gruber, Ph.D., Hank Wei, Ph.D., Richard Risser, M.S., Mauricio F. Tohen, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to identify domains of cognitive improvement for mania patients after 47 weeks of olanzapine treatment.

Summary:

Background: Patients with bipolar disorder have demonstrated a range of cognitive deficits involving executive control, attention, memory, and psychomotor speed. These deficits can be persistent even with improvement in affective symptoms. The current study examined changes in cognitive performance in a cohort of bipolar patients.

Methods: Patients experiencing an acute manic episode (N=142) were enrolled in a multisite, double-blind, randomized clinical trial of either olanzapine or divalproex and were evaluated at baseline, seven weeks, and 47 weeks of treatment. Typical clinical rating scales as well as a brief battery of neurocognitive measures were administered.

Results: Change scores from baseline to week 47 showed significant improvement for olanzapine compared to divalproex on the Young Mania Rating Scale total score (p=.006). Change scores from baseline to week 47 showed significant improvement for olanzapine compared to divalproex for the Controlled Word Association Test (p=0.006) and number of perseverative errors on the Wisconsin Card Sorting Test (p=0.046).

Conclusion: Improvement on these two neurocognitive measures suggests an increased ability to maintain mental set and generate appropriate responses. These findings indicate that long-term treatment with olanzapine is associated with improved cognitive performance in patients with bipolar disorder, specifically those experiencing a manic episode.

Funding Source(s): Eli Lilly and Company

References:

NR813 Wednesday, May 5, 3:00 p.m.-5:00 p.m. A New Biological Marker for Creutzfeldt-Jakob Disease

Aron D. Mosnaim, Ph.D., Department of Pharmacology, FUHS, The Chicago Medical School, 3333 Green Bay Road, North Chicago, IL 60064; Maria A. Valenzuela, Ph.D., Ana Kettlun, Ph.D., Luis Cartier, M.D., Lucia Collados, Pharm.D., Lorena Garcia, Pharm.D., Marion E. Wolf, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize a new biological marker for Creutzfeldt-Jakob Disease and its possible implication in the pathophysiology of this condition.

Summary:
The growing interest in prion-induced diseases has stimulated research in the field of CJD.

Objectives: This study was designed to determine whether the CSF matrix metalloproteinase (MMP) profile could be useful as a biological marker for CJD.

Methodology: We determined in 16 subjects with CJD and in 16 age, and sex-comparable controls the presence of MMP-2 and MMP-9 in their active and proenzyme forms, the relative levels of MMP-3, the effects of four inhibitors of MMPs activity (TIMP-1, TIMP-2, TIMP-3 and TIMP-4), and the concentration of the 14-3-3-protein, using zymography and immunological techniques.

Results: Data obtained indicate that CJD patients, in comparison to controls, have a significantly higher positive frequency of pro-MMP-9 and of the active form of MMP-2, along with significantly higher levels of TIMP-1 and TIMP-2, classical inhibitors of MMP-9 and MMP-2, respectively. We also found a positive correlation between the 14-3-3 protein concentration (a useful diagnostic tool in CJD), and that of TIMP-1 and TIMP-2 levels.

Discussion: Current literature indicates that endogenous MMP cleavage of normal and disease associated isoforms of the human prion give rise to peptides of different size. Moreover, the profile of endogenous proteolytic PrPsc peptides appears to be characteristic for various CJD subtypes, thus allowing the molecular classification of this prion disease.

Conclusions: Data analysis in the context of these findings would suggest that MMPs may have a pathophysiological role in...
VN, and that their particularly profile may constitute a useful biological marker for this condition.

**Funding Source(s):** Grant Fondecyt 1000-854

**References:**


**NR814 Wednesday, May 5, 3:00 p.m.-5:00 p.m.**

**Alcohol Consumption in MDD and Its Relationship With Sleep Disturbances**

Alessandra Mascarini, M.D., Depression and Clinical Research Program, Mass. General Hospital, 50 Staniford Street, 4th Floor, Boston, MA 02114; Eliana Tossani, Ph.D., John J. Worthington III, M.D., Alana M. Burns, B.A., Andrew A. Nierenberg, M.D., Maurizio Fava, M.D.

**Educational Objectives:**

At the conclusion of this session, the participant should be able to assess the relationship between alcohol consumption and sleep disturbances among major depressive disorder outpatients participating in an antidepressant treatment study.

**Summary:**

**Objective:** We wanted to assess the relationship between alcohol consumption and sleep disturbances among major depressive disorder (MDD) outpatients participating in an antidepressant treatment study.

**Method:** 129 outpatients (57% women, mean age: 37.2 ± 11.1) with MDD diagnosed by SCID were recruited for a treatment study. Their severity of depression and sleep disturbances was assessed with the 28-item Hamilton Rating Scale for Depression (HAM-D-28), while their alcohol intake was assessed with a clinician-rated consumption habit questionnaire. Patients with current alcohol or substance abuse/dependence were excluded from the study. The relationship between alcohol consumption (in ounces per week) and sleep disturbance items of the HAM-D-28 was assessed with two separate multiple linear regressions, one with the three insomnia items and one with the three hypersomnia items.

**Results:** The mean alcohol consumption in our sample of depressed outpatients was 2.7 ±4.6 (range: 0-30) ounces of alcohol per week. We found no significant relationship between alcohol consumption and age, gender, or severity of depression (as measured by the HAM-D-28). While there was no significant relationship between HAM-D-28 insomnia items and alcohol consumption, there was a significant (p<0.05) relationship with daytime napping and a trend toward a significant relationship (p=0.08) with oversleeping at night (e.g., sleeping past the usual waking time).

**Conclusion:** While alcohol consumption did not appear to be related to severity of insomnia symptoms, the degree of alcohol consumption was found to be associated with oversleeping and napping. Further studies need to evaluate the nature of this relationship.

**Funding Source(s):** Lichtwer

**References:**


**NR815 Wednesday, May 5, 3:00 p.m.-5:00 p.m.**

**Efficacy and Tolerability of Controlled-Release Paroxetine to Treat Severe Depression Supported by GlaxoSmithKline**

Philip D. Perera, M.D., Psychiatry Department, Glaxo-Smith Kline, 2301 Renaissance Boulevard, King of Prussia, PA 19406; Cornelius D. Pitts, R.P.H., Alan Lipschitz, M.D., Julie Christie, M.S.

**Educational Objectives:**

At the conclusion of this session, the participant should be able to understand the efficacy of controlled-release paroxetine in severe and non-severe depression.

**Summary:**

**Objective:** To determine the efficacy and tolerability of paroxetine controlled release (CR) in the treatment of severely depressed patients.

**Method:** Data were pooled across four, double-blind, placebo-controlled studies of paroxetine. CR (12.5-62.5 mg) in major depression (n=1083). Patients were categorized according to their baseline Hamilton Depression Rating Scale (HAM-D) total score as having severe (>25) or non-severe (<25) depression. Symptom changes were assessed based on mean change in HAM-D total scores and the proportion of responders (CGI-global improvement score of 1 or 2) at last observation carried forward (LOCF) endpoint.

**Results:** At study endpoint, statistically significant improvements in depressive symptoms were observed for paroxetine CR relative to placebo in patients with severe depression (-4.37, 95% CI (-6.31, -2.42), p=0.0001), and non-severe depression (-1.89, 95% CI (-2.91, -0.87), p=0.0003). The odds of responding (CGI global improvement score of 1 or 2) were also significantly higher for patients receiving paroxetine CR than those receiving placebo in both severity categories (OR =2.42, 95% CI (1.50, 3.91), P=0.0003; OR =1.83, 95% CI (1.21, 2.19), p=0.0013, severe and non-severe depression, respectively). Withdrawal rates due to adverse events were 9.8% versus 5.4% (severe) and 5.2% versus 4.5% (non-severe), paroxetine CR and placebo, respectively.

**Conclusion:** These data demonstrate that paroxetine CR is effective and well tolerated in patients with severe depression as well as non-severe depression.

**Funding Source(s):** GlaxoSmithKline Pharmaceuticals

**References:**


**NR816 Wednesday, May 5, 3:00 p.m.-5:00 p.m.**

**The Economic Consequences of Treatment Discontinuation: Paroxetine Controlled Release Versus Paroxetine Immediate Release Supported by GlaxoSmithKline**

David V. Sheehan, M.D., Department of Psychiatry, University of South Florida, 3515 East Fletcher Avenue, Tampa, FL.
NR818  Wednesday, May 5, 3:00 p.m.-5:00 p.m.
Effect of Duloxetine on Sexual Functioning During Treatment of MDD
Supported by Eli Lilly and Company
Fujun Wang, Ph.D., Statistics, Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285; Madelaine M. Wohlreich, M.D., Michael J. Defke, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be aware that during 12 weeks of duloxetine therapy, patients exhibited significant reduction (improvement) in mean PGI-SF score and during an additional 26 weeks of therapy, changes in sexual functioning did not differ significantly from that observed in patients switched to placebo.

Summary:
Background: Sexual dysfunction is highly prevalent in patients with major depressive disorder (MDD), and is also frequently encountered as a treatment-emergent side effect associated with antidepressant therapy. Changes in sexual functioning during acute and long-term treatment with duloxetine were assessed using a patient-rated scale.

Methods: Patients with MDD received open-label duloxetine (60 mg QD; N=533) for 12 weeks. Treatment responders were subsequently randomized to receive duloxetine (60 mg QD; N=136) or placebo (N=142) for an additional 26 weeks. Sexual functioning was assessed using the four-item Patient Global Impression of Sexual Function (PGI-SF) scale (sexual interest/desire, vaginal lubrication/erectias; orgasm, overall sexual function).

Results: During acute-phase, open-label duloxetine therapy, mean changes for all four PGI-SF items exhibited significant reduction (improvement) from baseline. When analyzed by gender, mean change among female patients showed significant improvement from baseline on all four items, while males had significant improvement in sexual interest/desire. In the 26-week, double-blind continuation phase, mean changes in PGI-SF from random-
Duloxetine Treatment of MOD in Hispanic and African-American Patients

NR819 Wednesday, May 5, 3:00 p.m.-5:00 p.m.
TMS Over Right DLPFC Improves Affective Set-Shifting in Patients With MDD

Felix Bermpoil, M.D., Behavioral Neurology, Beth Israel Deaconess Medical College, 330 Brookline Avenue, KS 454, Boston, MA 02215; Felipe Fregni, Paulo S. Boggio, M.S.C., Georg Northoff, M.D., Sergio P. Riconatti, M.D., Marco A. Marcolin, Ph.D., Alvaro Pascual-Leone, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to have improved understanding of the pathophysiology underlying major depression.

Summary:
Major depressive disorder is characterized by affective and cognitive symptoms. Cognitive deficits can, for example, be objectified in attentional set-shifting tasks. Neuroimaging studies reveal prominent deactivation in the left dorsolateral prefrontal cortex (DLPFC) during acute depressive episodes. Following successful antidepressant treatment this abnormality normalizes.

The present study investigated, using TMS, the role of the right and left DLPFC for affective set-shifting deficits in major depression.

Patients with unipolar major depression were compared with remitted depressive patients and healthy control subjects. Affective set-shifting deficits were assessed using the Affective Shifting Task (AST). 1 Hz TMS (60% of maximum output; 10 min) was used to transiently suppress activity in right DLPFC, left DLPFC and occipital cortex (control condition). After each TMS session the AST was performed. Patients with acute major depression significantly improved in affective set-shifting after TMS over the right DLPFC, while TMS over the left DLPFC had no effect compared to occipital TMS. In contrast, both healthy subjects and remitted patients showed impaired performance following TMS over the left DLPFC.

Our findings suggest that an imbalance between left and right DLPFC activity might contribute to affective set-shifting deficits in patients with major depressive disorder.

Funding Source(s): German Academic Exchange Service (DAAD)

References:

NR820 Wednesday, May 5, 3:00 p.m.-5:00 p.m.
Duloxetine Treatment of MDD in Hispanic and African-American Patients
Supported by Eli Lilly and Company

John M. Plewes II, M.D., Neuroscience Department, Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285; Rahn K. Bailey, M.D., Craig H. Mallinckrodt, Ph.D., John G. Watkin, D.Phil., Madelaine M. Wohlreich, M.D., Roberto Lewis-Fernandez, M.D.

Educational Objectives:
At the conclusion of this session, participant should learn that the efficacy and safety of duloxetine (40–120 mg/d) in cohorts of Hispanic and African American patients was comparable to that observed in Caucasian patients.

Summary:
Objective: To assess the safety and efficacy of duloxetine, a balanced and potent dual reuptake inhibitor of serotonin and nor-epinephrine, in the treatment of major depressive disorder (MDD) in US-resident patients of Hispanic, African, or Caucasian descent.

Methods: Efficacy and safety data were pooled from seven double-blind studies. Patients (Hispanic, n=120; African American, n=128; Caucasian, n=1342) received duloxetine (60 mg QD or 20, 40, or 60 mg BID) or placebo for up to nine weeks.

Results: Mean changes in principal efficacy measures (HAM-D, CGI-S, PGI-I) were similar in all three ethnic groups. Discontinuation rates due to adverse events were 14.0% for Hispanics, 13.0% for African Americans, and 17.0% for Caucasians, while the event most frequently leading to discontinuation in each group was nausea (3.4%, 1.4%, and 2.3%, respectively). The most common treatment-emergent adverse events were similar between ethnic groups and included nausea, dry mouth, constipation, headache, diarrhea, and dizziness. In each ethnic group, mean changes from baseline for pulse, blood pressure, and laboratory analytes were small, and the rate of abnormal values was low.

Conclusion: Duloxetine (40–120 mg/d) was shown to be similarly efficacious, safe and well-tolerated for the treatment of MDD in cohorts of Hispanic, African-American, and Caucasian patients.

Funding Source: Eli Lilly and Company

References:

NR821 Thursday, May 6, 12:00 p.m.-2:00 p.m.
Using Life to Assess Outcomes in Bipolar Disorder: Reliability and Validity

Sagar V. Parikh, M.D., Department of Psychiatry, University of Toronto, 399 Bathurst Street, Toronto, ON M5T 2S8, Canada; Vytas Velyvis, M.A., Aleda Franz, B.A.

Educational Objectives:
At the conclusion of this session, the participant should: (1) understand the variability in symptom course for bipolar disorder over the span of a year; (2) discover how the LIFE can be used as tool for assessing symptom course in longitudinal research; (3) identify difficulties and find solutions for training other sites in using the LIFE.
NR822 Thursday, May 6, 12:00 p.m.-2:00 p.m.
Personality Changes in Alzheimer’s Disease

Angie Boding, Ruan Neurology, 1111 6th Avenue West Building, Suite 400, Des Moines, IA 50314; Jim Andrikopoulos, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize personality changes associated with Alzheimer’s disease.

Summary:
Hypothesis: Personality changes are seen early in the course of Alzheimer’s disease, often co-occurring with the cognitive impairment. Identifying these changes may assist in an early diagnosis. The purpose of this study was to develop an empirically based caregiver questionnaire for identifying personality changes associated with Alzheimer’s disease.

Methods: Family members of patients with Alzheimer’s disease (N=260) were asked to complete a 40-item personality inventory inquiring about personality changes in the patient. The initial pool of questions were derived from a review of the literature describing common personality changes seen in Alzheimer’s disease.

Results: A principal components factor analysis yielded a 21-item, four-factor solution: Agitation, anhedonia, psychosis, and anxiety factors accounted for 34% of the variance. The symptoms most commonly endorsed by caregivers reflected depressive symptoms: depressed (59.1%); lack of energy (54.9%); lack of interest (49.2%); excessive worrying (44.3%); and a change in social activities (35.2%).

Conclusions: The personality items endorsed by caregivers were primarily composed of neurovegetative symptoms, often interpreted as signs of depression or an anxiety disorder by family members. These personality changes are said instead to reflect the neurovegetative organic changes related to the disease, versus major depression per se.

References:

NR823 Thursday, May 6, 12:00 p.m.-2:00 p.m.
Pilot Study Evaluating the Use of Rivastigmine in Patients With Mixed Dementia
Supported by Novartis Pharmaceuticals Corporation

Ibrahim Gunay, M.D., USCD & MA CNS, Novartis Pharma Corporation, One Health Plaza, East Hanover, NJ 07936; Barbara Kounaras, Michael Chen, Ph.D., Dario F. Mirski, M.D.

Educational Objectives:
At the conclusion of this session, the participant will know there is an ongoing pilot study of rivastigmine use in mixed dementia.

Summary:
Introduction: Alzheimer’s disease (AD) is currently the most prevalent form of dementia (60% of cases). Vascular dementia (VaD) accounts for 10% to 20% of cases. It is estimated that AD and VaD frequently coexist in mixed dementia (10% to 20% of cases). Mixed dementia includes patients with a diagnosis of AD with concurrent cerebrovascular lesions, and also patients who present with clinical features of VaD and AD.

Methods: Interim analysis of the demographic data from an ongoing open-label, multicenter study assessing the safety/efficacy of rivastigmine 3–12mg/day in patients with mixed dementia. The presence of VRFs was determined by the Modified Hachinski Ischemic Score (MHIS). Patients were stratified according to baseline MHISs (no vascular risk factors; MHIS=0, vascular risk factors; MHIS>0).

Results: One-hundred nineteen patients are included in the demographics analysis, sixty-three males and fifty-six females. 62 patients had MHIS<4, 57 patients had MHIS>4. 82% had hypertension and 57% had hypercholesterolemia. 73% of patients did not have diabetes, 67% did have cerebrovascular disease. 90% of patients had a cardiac disorder, and 33% had vascular disease.

Conclusion: These demographic results present a mixed dementia population. Baseline demographic results of patients categorized by MHIS showed no significant behavioral differences between groups.

Funding Source(s): Novartis Pharmaceuticals Corp.

References:
NR824 Thursday, May 6, 12:00 p.m.-2:00 p.m.

**Pilot Study of Galantamine Versus Donepezil in Mild to Moderate Alzheimer’s Disease**

*Supported by Janssen Pharmaceutica and Research Foundation*

Sonia Ancoli-Israel, Ph.D., Psychiatry Department, University of California, San Diego, 9500 Gilman Drive, La Jolla, CA 92093-9116; Joan Amatniek, M.D.

**Educational Objectives:**

At the conclusion of this session, the participant should be able to discuss the different treatment effects of galantamine and donepezil in patients with mild to moderate AD.

**Summary:**

**Objectives:** To explore differences in efficacy and safety between donepezil and galantamine, an allosteric nicotinic receptor modulator and acetylcholinesterase inhibitor, in mild to moderate Alzheimer's disease (AD).

**Methods:** In this double-blind pilot study patients were randomized 1:1 to galantamine 16 mg/day (n=31) or donepezil 10 mg/day (n=32) for eight weeks according to recommended dosing and titration schedules. Assessments included the Clinician's Interview-Based Impression of Change Plus Family Input (CIBIC-plus) and adverse event (AE) reporting. Other assessments included sleep quality, attention, and quality of life measures.

**Results:** 27 galantamine and 29 donepezil patients were administered the CIBIC-plus at baseline and Week 8. All galantamine patients improved or exhibited no change, none worsened; 25 donepezil patients (86.2%) improved or exhibited no change while 4 (13.8%) worsened. 21 patients (67.7%) randomized to galantamine and 17 (53.1%) receiving donepezil reported at least one AE. Rates of gastrointestinal AEs were similar between treatments (occurring in five galantamine and five donepezil patients). As expected from mechanisms of action, galantamine patients experienced slightly more nicotinic-related AEs, and donepezil patients experienced more muscarinic-related AEs.

**Conclusion:** In this pilot study, more patients receiving galantamine exhibited improved or maintained global function than those receiving donepezil. Both treatments were similarly well tolerated.

**Funding Source(s):** Janssen Pharmaceutica Products, LP.

**References:**


NR825 Thursday, May 6, 12:00 p.m.-2:00 p.m.

**Effect of Galantamine Versus Donepezil on Sleep Quality in Mild to Moderate Alzheimer’s Disease**

*Supported by Janssen Pharmaceutica and Research Foundation*

Sonia Ancoli-Israel, Ph.D., Psychiatry Department, University of California, San Diego, 9500 Gilman Drive, La Jolla, CA 92093-9116; Phyllis Zee, M.D., Steve Ascher, Ph.D., Joan Amatniek, M.D.

**Educational Objectives:**

At the conclusion of this session, the participant should be able to evaluate the different effects of galantamine and donepezil on sleep quality in patients with mild to moderate AD.

**Summary:**

**Objectives:** The poor sleep quality of AD adversely affects caregiver and patient functioning. This study compared the effects of galantamine and donepezil on sleep in mild to moderate AD patients, while exploring subjective and objective methods for measuring sleep in these patients.

**Methods:** This double-blind pilot study randomized patients 1:1 to galantamine 16 mg/day (n=31) or donepezil 10 mg/day (n=32) for eight weeks according to recommended dosing and titration schedules. Sleep measurements included actigraphy (Actiwatch), Pittsburgh Sleep Quality Index (PSQI), and Circadian Sleep Inventory for Normal and Pathological States (CSINIPS). A composite sleep score derived from 10 sleep-related components from actigraphy, PSQI, CSINIPS and safety data were used to assess sleep quality, thereby permitting the use of sleep medications as necessary.

**Results:** Actiwatch data evaluated sleep percentage, number of sleep and wake bouts, and sleep and wake bout times. Actiwatch and PSQI data were obtained for patients and caregivers. Preliminary results indicate that PSQI and composite measures showed more between-group differences than Actiwatch data, with a pattern suggesting that galantamine patients reported better sleep quality than those receiving donepezil.

**Conclusion:** A larger study may be warranted to determine the differential impact of these therapies on sleep quality in AD patients.

**Funding Source(s):** Janssen Pharmaceutica Products

NR826 WITHDRAWN

NR827 WITHDRAWN

NR828 Thursday, May 6, 12:00 p.m.-2:00 p.m.

**Galantamine Treatment of Vascular Dementia: Patient Characteristics**

*Supported by Janssen Pharmaceutica and Research Foundation*

Elisabeth Van Straaten, M.D., VU Medical Center, de Boelelaan 1117, Amsterdam 1007, Netherlands; Alexander P. Auchus, M.D., Frederik Barkhof, M.D., H. Robert Brashear, M.D., Philip Scheltens, M.D.

**Educational Objectives:**

At the end of this presentation, the participant should be able to understand the characteristics of a study population with probable vascular dementia (VaD) with standardized radiological confirmation.

**Summary:**

**Objective:** Galantamine, previously studied in patients with AD+CVD or probable VaD, had beneficial cognitive, global, behavioral, and functional effects. The current trial was designed to evaluate the efficacy of galantamine in a population of probable VaD patients.

**Methods:** This six-month, multicenter, double-blind trial included patients diagnosed with probable VaD according to NINDS-AIREN...
A central imaging laboratory evaluated MRI scans to confirm objective radiologic criteria for CVD. Eligible patients were randomized to placebo or galantamine (8 or 12 mg b.i.d.). Efficacy measures for cognitive and executive functioning were the ADAS-Cog/11 and EXIT-25.

Results: 1,737 patients were screened, 787 randomized to treatment. Mean baseline scores were: ADAS-Cog 22.7 (range 5-62) and Exit 25 18.7 (range 3-37). The most frequent cause of exclusion was insufficient CVD to meet NINDS-AIREN radiologic criteria. All 787 randomized subjects had objective evidence of CVD (territorial infarcts, lacunes, severe white matter disease) with over 2/3 having two or more lesion types.

Conclusions: Previous VaD trials may have included significant numbers of “subjects with AD+CVD”. This trial enrolled patients with a high degree of cerebrovascular burden and a wide range of impairment in cognitive and executive function, representing a relatively “pure” VaD population.

References:

NR829 Thursday, May 6, 12:00 p.m.-2:00 p.m.
Retrospective Analysis of Risk Factors in Olanzapine Clinical Trials in Elderly Dementia Patients Supported by Eli Lilly and Company
Vicki P. Hoffmann, Pharm.D., Neuroscience Department, Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285; Thomas Hardy, M.D., Jonna Ahl, Ph.D., Ilya Lipkovich, Ph.D.

Educational Objectives:
At the conclusion of this session, participant should be able to understand that elderly patients with dementia may be at risk of developing diabetes if they have elevated glucose levels.

Summary:
Purpose: To determine the risk of diabetes in elderly patients with dementia who are receiving antipsychotic medication.
Methods: The olanzapine dementia clinical trial database was surveyed for treatment-emergent diabetes (TED) in patients over 65 years of age (elderly). TED was defined as having two post baseline random glucose values ≥200 mg/dL, or initiation of antidiabetic medication, or clinical diagnosis of diabetes. Risk factors evaluated: age, ethnicity, hypertension, baseline body mass index (BMI) ≥25, maximum baseline glucose ≥140 mg/dL.

Results: Seven studies included elderly patients without preexisting diabetes (n=1461), who received olanzapine (n=875), an active comparator (n=24), or placebo (n=343). Mean treatment exposure was 130 days, 179 days, and 116 days, respectively. Patients with TED (n=40) had similar mean BMI and mean age as those patients without TED. Elevated baseline glucose (≥140 mg/dL) correlated significantly with the development of TED. Number of risk factors, individual risk factors, and treatment were not predictive of TED.

Conclusions: Only baseline blood glucose levels, irrespective of treatment, were significantly correlated with TED. Elderly dementia patients should be assessed for risk of diabetes before antipsychotic therapy is begun.

Funding Source: Eli Lilly and Company

References:

NR830 Thursday, May 6, 12:00 p.m.-2:00 p.m.
A Wellness Intervention Program for Patients With Serious and Persistent Mental Illness Supported by Eli Lilly and Company
Vicki P. Hoffman, Pharm.D., Department of Neuroscience, Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285; Lara Jensen, M.S., Jacques Thierry, Jonna Ahl, Ph.D.

Educational Objectives:
At the conclusion of this session, participant should be able to discuss the benefits of wellness intervention programs for persons with serious and persistent mental illnesses.

Summary:
Objective: Obesity is prevalent in patients with serious and persistent mental illness (SPMI), and they have substantial risk for weight gain during psychopharmacological treatment. Obesity is difficult to reverse, but behavioral programs involving diet and exercise have been successful sometimes. Solutions for Wellness Personalized Program provided individualized education and support for improving overall wellness.

Methods: Patients with any SPMI treated with any antipsychotic medication and living in the community were enrolled voluntarily. Participants completed an enrollment survey that provided information for the creation of individualized weight management plans that included nutrition, exercise, stress management, and sleep improvement. Weight and body mass index (BMI) were assessed at baseline and monthly for 6 months. Behavior and attitudes were assessed regularly.

Results: Over 7000 patients were enrolled. BMI at baseline was ≥25 in 83% of the participants. After 6 months, participants (n=3,341) reported positive changes in diet (90.2%), exercise (85.0%), handling stress (93.8%), and improved sleep (92.9%). Those individuals who made positive changes in diet, also reported weight loss and reduced BMI (~0.93 kg/m², mean change). In addition, 97% of participants reported having gained confidence in the ability to maintain lifestyle changes.

Conclusions: Patients suffering from SPMI reported positive changes in diet, exercise, handling stress, improved sleep, and increased confidence in maintaining lifestyle changes after participating in the Solutions for Wellness Personalized Program. Healthy living interventions should be considered part of an overall treatment plan for patients with SPMI.

Funding Source: Eli Lilly and Company

References:

NR831 Thursday, May 6, 12:00 p.m.-2:00 p.m.
Memantine Is Safe for Short- and Long-Term Treatment of Dementia Supported by Forest Laboratories, Inc.
Stephen Graham, Ph.D., Forest Research Institute, Plaza Five Harborside Financial Center, Jersey City, NJ 07311; Jeffrey

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Jonas, M.D., Grace S. Lee, B.A., Magaret A. Goetz, M.P.H., Albrecht Stoffler, M.D., Yvonne Wirth, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to evaluate the short- and long-term safety and tolerability of memantine for the treatment of dementia.

Summary:
Memantine, an NMDA-receptor antagonist, has been approved in the U.S. for moderate-to-severe Alzheimer's disease (AD). Short- and long-term safety of memantine for dementia were assessed.

Short-term safety in moderate-to-severe AD patients (n=734; memantine 10–20mg/day; 12–28 weeks) was assessed in three of five double-blind placebo-controlled trials. Two of five trials examined mild-to-moderate vascular dementia (VaD) patients (n=900; memantine 20mg/day; 28 weeks). Long-term safety was assessed from four open-label extension studies with AD and VaD patients (n=856; memantine 20mg/day; 24–104 weeks). Safety parameters included adverse events (AEs), vital signs, clinical laboratory tests.

Short-term safety: only headache and confusion were reported in ≥5% of moderate-to-severe memantine-treated AD patients at an incidence of at least twice that of placebo. Only constipation was reported in ≥5% of memantine-treated VaD patients at an incidence of at least twice that of placebo. Long-term safety: AEs reported by ≥5% of memantine-treated patients were agitation, urinary tract infection, fall, inflicted injury and dizziness (all ≤7%). Most AEs reported in all studies were considered mild or moderate in severity and not related to memantine. No clinically relevant differences between memantine and placebo patients in vital signs or laboratory values were observed.

Short- and long-term dementia treatment with memantine is safe and well-tolerated.

Funding Source(s): Forest Laboratories, Inc. and Merz Pharmaceuticals GmbH

References:

NR832 Thursday, May 6, 12:00 p.m.-2:00 p.m.
Predictors of Cognitive Decline in an Older Korean Population

Sang Hoon Kim, M.D., Department of Psychiatry, Chosun University, 588 Seosukdong Dong-Gu, Gwangju City 510-717, Korea; Jae Min Kim, M.D., Sang-Hag Park, Hack-Ryul Kim

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the factors affecting cognitive decline in old persons, and the interaction between gene (apolipoprotein E ε4) and environment (education) in this regard.

Summary:
Objectives: This study aimed to investigate factors that predict cognitive decline in an older Korean population.

Methods: A community cohort (n=683) aged 65 or over completed the MMSE at baseline and two years later (1999–2001) in Kwangju, South Korea. Uni- and multivariate associations of decline on the MMSE with demographic (age, gender, education, urban/rural living, family history of dementia), lifestyle (smoking, alcohol drinking, eating pattern), clinical (MMSE, depression, sleep disorder), and biological (vascular risk/disease, apolipoprotein E genotype) characteristics at baseline were measured using linear regression.

Results: In the univariate analyses, cognitive decline was associated with advanced age, female gender, higher score on MMSE at baseline, insomnia, vascular risk factors, and apolipoprotein E ε4. In the multivariate analyses, cognitive decline was associated with advanced age, higher score on MMSE-K at baseline, and apolipoprotein E ε4. The interaction of education with apolipoprotein E ε4 was observed (p=0.040), while that with other factors were not. The association between apolipoprotein E ε4 and cognitive decline was only apparent in the old persons with no education.

Conclusion: Populations with no education were particularly vulnerable to the impact of apolipoprotein E ε4 on cognitive decline apolipoprotein E ε4 and education.

References:

NR833 Thursday, May 6, 12:00 p.m.-2:00 p.m.
Mood and Menstrual Cycle in Bipolar Disorder: A Time-Series Approach

Natalie L. Rasgon, M.D., Department of Psychiatry, Stanford University, 401 Quarry Rd, Room 2360, Palo Alto, CA 94305-5723; Michael Bauer, M.D., Paul Grof, M.D., Tom Bschor, M.D., Laszlo Gyulai, M.D., Tasha Glenn, Peter C. Whybrow, M.D.

Educational Objectives:
At the conclusion of this session, the participant should know more about using time series analysis to investigate the relation between mood and menstrual cycle.

Summary:
Objective: Investigation of the relation between mood and menstrual cycle in women with bipolar disorder has shown mixed results. This study uses a time series approach to analyze the relation between mood and menstrual cycle in women receiving treatment for bipolar disorder.

Method: Eight women (5 BP I; 3 BP II) using ChronoRecord software to self-report mood, sleep, menstrual cycle, and medications were selected for having a minimum of 150 days of data, and two sequential missing days or less. Auto-correlation was used to determine patterns of mood change and harmonic regression was used to confirm cycle length.

Results: In two patients (both BP II) there was a significant (> twice standard error), positive, autocorrelation using both the raw mood data and first difference of mood data, showing a clear cyclical pattern in mood with a cycle length that matched the mean menstrual cycle length. Harmonic regression analysis confirmed the cycle length for both patients. In both cases, the standard error of the regression was minimized at the mean menstrual cycle length. No significance was found for the other six patients.

Conclusions: A time series approach can identify women with cyclical mood patterns related to the menstrual cycle.
References:

NR834 Thursday, May 6, 12:00 p.m.-2:00 p.m.
Assessment of Respiratory Effects of Indiplon-MR Supported by Neurocine Biosciences, Inc.
Martin Cohn, M.D., Sleep Disorders Center of SW Florida, 11181 Health Park Boulevard, Naples, FL 34110; Philip Jochelson, M.D., Noelle Gately, B.A., Cara Baron, M.S., Michele Boyd

Educational Objectives:
The research data presented in this poster will increase the participant’s knowledge of the respiratory safety during sleep of indiplon-MR, a new investigational treatment for insomnia.

Summary:
Objective: To evaluate the respiratory effects of modified release indiplon, a GABA-A potentiator, following CO2 challenge.
Methods: 12 healthy male volunteers (mean age, 32 yrs) were randomized, in a double-blind crossover study, to treatment with a single dose of indiplon-MR 30 mg, codeine sulfate 60 mg, or placebo. Ventilatory and mouth occlusion pressure responses to carbon dioxide challenge, and arterial oxygen saturation (SaO2), were measured 1 h before and at 1, 2, 4, 6, 8 h after dosing.

Results: Indiplon-MR had no statistically or clinically significant effects on respiratory function compared with placebo as assessed by minute ventilation (Ve) in response to CO2 challenge, mouth occlusion pressure in response to CO2 challenge, resting mean inspiratory flow at pre-CO2 challenge, resting end tidal PCO2 of expired air at pre-CO2 challenge, and SaO2. Following treatment with codeine sulfate 60 mg, respiratory suppression on Ve was observed in response to CO2 challenge at all post-dose timepoints, with the most notable reductions from mean pre-dose values observed at 1 h and 6 h post-dose. Indiplon was well tolerated.

Conclusions: The 30 mg dose of indiplon-MR was safe and well-tolerated, with no clinically significant effect on respiratory drive in healthy volunteers following CO2 challenge.

References:

NR835 Thursday, May 6, 12:00 p.m.-2:00 p.m.
Does Automated Self-Reporting Bias Data From Patients With Bipolar Disorder?
Michael Bauer, M.D., Department of Psychiatry, Charite University Hospital, Humboldt University Schumannstr 20121, Berlin 10117, Germany, Natalie L. Rason, M.D., Paul Grof, M.D., Laszlo Gyulai, M.D., Tasha Glenn, Peter C. Whybrow, M.D.

Educational Objectives:
At the conclusion of this session, the participant should better understand the relation between using technology for data collection in longitudinal studies and sample bias.

Summary:
Objective: Automation of data collection can improve data quality, enhance patient compliance and decrease the costs of longitudinal studies. While we previously validated ChronoRecord software for self-reporting mood on a home computer, this study further investigates if this technology creates a bias in the collected data.

Methods: During the validation study, 80 of 96 (83%) patients with bipolar disorder returned 8662 days of data (mean days 114.7 ± 32.3 SD). Since demographic characteristics may influence feelings about technology, observer-rated scores on HAMD and YMRS were used to group the patients by severity of illness and the self-reported mood ratings were analyzed for evidence of bias from the patients’ gender, ethnicity, diagnosis, age, disability status or years of education. The analysis used two-way ANOVA and general linear models. Patient demographic characteristics were also compared to those from similar longitudinal studies that used paper-based data collection tools.

Results: After grouping by severity of illness, none of the demographic variables had a significant effect on the patients’ self-reported mood using the automated tool. The patients’ demographics were very similar to those reported for patients with bipolar disorder who participated in longitudinal studies using paper-based self-reporting tools.

Conclusion: The use of a computer does not appear to bias the sample data.

References:

NR836 Thursday, May 6, 12:00 p.m.-2:00 p.m.
Mood and Sleep in Patients Treated for Bipolar Disorder: A Time-Series Approach
Michael Bauer, M.D., Department of Psychiatry, Charite University Hospital, Humboldt University Schumannstr 20121, Berlin 10117, Germany, Natalie L. Rason, M.D., Paul Grof, M.D., Tomi Bschor, M.D., Laszlo Gyulai, M.D., Tasha Glenn, Peter C. Whybrow, M.D.

Educational Objectives:
At the conclusion of this session, the participant should know more about the relation between sleep and mood in patients receiving treatment for bipolar disorder.

Summary:
Objective: Sleep disturbances commonly accompany mania and depression. This study verifies these changes in medicated patients, using daily self-reported mood and sleep data from patients receiving a mean of 3.8 medications daily.

Method: 60 patients (41 BP I; 19 BP II), entering data for a mean of 149 days into ChronoRecord software, were selected for having 2 or less sequential days of missing data. Per patient, mood and sleep data was pre-whitened using an ARIMA (0, 1, 1) model to remove trends and establish stationarity. The relationship between mood and sleep over time was determined using cross-
correlation analysis. By diagnosis, patients with and without significant cross-correlations were compared using a univariate linear mixed model.

Results: 23 patients (16 BP I, 7 BP II) showed significant inverse cross-correlations between mood and sleep at a lag of 0; 37 patients (25 BP I, 12 BP II) did not. Those showing significance were manic/hypomanic (p=.011) more frequently, had more severe symptoms of mania (p=.041), more switches from normal to mania/hypomania (p=.029), mania/hypomania to depression (p=.006), depression to mania/hypomania (p=.015), took more medications (p=.002) and were disabled more often (p=.037).

Conclusions: Despite multiple medications, patients symptomatic for bipolar disorder still have sleep disturbances when manic or depressed.

References:

NR837 Thursday, May 6, 12:00 p.m.-2:00 p.m.
Efficacy and Tolerability of Indiplon Immediate Release in Transient Insomnia
Supported by Neurocine Biosciences, Inc.

Thomas Roth, Ph.D., Henry Ford Sleep Disorders Center, 2799 West Grand Boulevard, CFP3, Detroit, MI 48202; Martin B. Scharf, Ph.D., Russell Rosenb, Ph.D., Alan Lankford, Ph.D., Theresa Alexander, B.S.

Educational Objectives:
The research data presented in this poster should improve the participant's knowledge of the clinical efficacy and tolerability of indiplon-IR, a new investigational therapy for insomnia.

Summary:
Objective: The efficacy of immediate-release indiplon, a GABA-A potentiator, was evaluated by polysomnography (PSG) in volunteers with experimentally induced transient insomnia using laboratory adaptation combined with a two-hour phase advance.

Methods: Healthy volunteers age 21-64 (N=593; 62% female; mean, 32 years) with normal sleep were randomized to double-blind treatment with a single nighttime dose of indiplon-IR (10mg or 20mg) or placebo. PSG assessments included latency to persistent sleep (LPS) and total sleep time (TST); subjective assessments included latency to sleep onset (LSO) and sleep quality (SQ); next day effects were evaluated by the Digit Symbol Substitution Test (DSST), Symbol Copying Test (SCT) and a Visual Analog Scale of sleepiness (VAS).

Results: LPS and LSO were significantly reduced (p<0.0001) on both 10mg and 20mg of indiplon-IR. TST was significantly increased for both doses (p<0.005). SQ was also significantly improved on both doses. There were no next-day effects as evidenced by a lack of difference between indiplon-IR and placebo on DSST, SCT, or VAS. Both doses were well tolerated with a comparable incidence of adverse events relative to placebo.

Conclusions: Indiplon-IR was effective in inducing sleep, increasing sleep duration, and improving overall sleep quality without next-day residual sedation in a model of transient insomnia.

Funding Source(s): Neurocine

References:

NR838 Thursday, May 6, 12:00 p.m.-2:00 p.m.
An Assessment of the Long-Term Efficacy and Safety of Eszopiclone Over 12 Months of Nightly Treatments in Patients With Chronic Insomnia Supported by Sepracor, Inc.

Thomas Roth, Ph.D., Henry Ford Sleep Disorders Center, 2799 West Grand Boulevard, CFP3, Detroit, MI 48202; Andrew D. Krystal, M.D., Thomas Wessel, M.D., Judy Caron, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to evaluate the long-term effects of eszopiclone on all measures of sleep and on daytime function.

Summary:
Objective: Insomnia agents are often used long-term to treat chronic insomnia, but long-term efficacy has not been demonstrated. Eszopiclone has demonstrated statistically significant improvements in measures of sleep and daytime function vs placebo for up to 6 months (Krystal, 2003). To evaluate continued efficacy and safety, the study included a 6-month open-label extension, presented here.

Methods: Following the six-month, double-blind portion, 471 patients (111 placebo, 360 eszopiclone) entered the extension and received open-label eszopiclone nightly. Endpoints were patient reported sleep (onset, maintenance, duration, quality) and daytime function (daytime alertness, physical well-being, and daytime ability to function [concentrate]), captured weekly using an interactive voice response system.

Results: Patients previously treated with placebo reported immediate and significant improvements in sleep and daytime functioning. Their data were not different from patients who previously received eszopiclone. These improvements in reports of sleep and daytime function were sustained for the entire six-month extension period. At the end of the extension, 86/111 patients had received eszopiclone for six months, and 296/360 patients for 12 months. There were no significant withdrawal adverse events upon discontinuation.

Conclusions: Eszopiclone provided sustained improvement in sleep and next day functioning in patients with chronic insomnia over 12-months of therapy.

Funding Source(s): Sepracor Inc.

References:

NR839 Thursday, May 6, 12:00 p.m.-2:00 p.m.
Sleep-Consolidating Effects of Tiagabine in Patients With Primary Insomnia
Supported by Cephalon, Inc.

Thomas Roth, Ph.D., Henry Ford Sleep Disorders Center, 2799 West Grand Boulevard, CFP3, Detroit, MI 48202; James K. Waish, Ph.D.
Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the therapeutic potential of tiagabine as a sleep-enhancing agent.

Summary:

Introduction: The selective GABA reuptake inhibitor (SGRI) tiagabine has been shown to have sleep-consolidating effects in the elderly. One aim of the present study was to assess the sleep-consolidating effects of tiagabine in subjects with primary insomnia.

Methods: This was a cross-over (Latin-Square), double-blind, placebo-controlled, study of tiagabine 4, 8, 12, 16 mg in adult subjects. Dose was administered for two consecutive nights with 5–12 day washout between treatment periods. Assessments included polysomnography and psychomotor performance (DSST). 58 subjects were randomized. A qualitative treatment-by-period interaction was apparent; thus efficacy data are presented from period 1 only (n=11-12 per treatment group).

Results: Significant reduction in wake after sleep onset (min) was observed (placebo 94.8, 4 mg 71.0, 8 mg 59.9 [p<0.04], 12 mg 61.4 [p<0.047], 16 mg 65.4). A dose-related increase in slow-wave sleep (7.1%, 10.8%, 14.8%, 25.6% [p<0.01], 28.8 [p<0.01]), and decreases in stage 1 (11.2%, 9.0%, 8.0%, 6.9%, 12.9%) and number of awakenings (11.0, 12.3, 9.2, 9.3, 8.9) were observed. Residual impairment in morning performance was present only for the 2 highest doses. Most commonly reported adverse events were dizziness (0%, 2%, 0%, 11%, 21%), nausea (0%, 0%, 0%, 7%, 16%), and somnolence (2%, 2%, 0%, 6%, 9%).

Conclusions: Tiagabine significantly consolidated sleep at ≥8 mg dose and enhanced “deeper” NREM stages of sleep. Tiagabine ≤8 mg was well tolerated without residual sedation. Further research in insomnia is warranted.

Funding Source(s): Cephalon

References:


NR840 WITHDRAWN

NR841 Thursday, May 6, 12:00 p.m.-2:00 p.m.
Safety of Indiplon-MR in Mild-to-Moderate COPD
Supported by Neurocine Biosciences, Inc.

Steven Hull, M.D., Vince Associates Research, 6600 College Boulevard, Suite 330, Overland Park, KS 66211; Charles Fogarty, M.D., Alejandro Chediak, M.D., Bradley Vince, D.O., Philip Joehlson, M.D., Noelle Gately, B.A.

Educational Objectives:

At the conclusion of this session, the participant should be able to improve the participant’s understanding of treating insomnia in COPD with indiplon-MR, a new investigational therapy for insomnia.

Summary:

Objective: This study evaluated the respiratory depressant effects, safety and tolerability of a 20 mg dose of indiplon-MR in patients with mild-to-moderate COPD.

Methods: 18 patients (56% female; mean age, 53 yrs; 78% with moderate COPD), completed a single-blind placebo lead-in, and were randomized, in a double-blind, two-way crossover design, to indiplon-MR 20-mg and placebo. Primary outcomes consisted of arterial oxygen saturation (SaO₂), and the respiratory disturbance index (RDI=total # apnea/hypopnea events divided by total sleep time). Sleep quality was assessed using a subjective sleep quality morning questionnaire.

Results: Mean whole night SaO₂ was similar for indiplon-MR (93.6%) vs. placebo (93.4%). No indiplon-MR vs. placebo difference was observed in SaO₂ during REM (93.0% vs. 92.8%) and non-REM sleep (93.0% vs. 92.9). Mean RDI was also similar for indiplon-MR (2.7 ± 0.7; max-RDI, 8.3) vs. placebo (3.2 ± 0.7; max-RDI, 10.0). Sleep quality was subjectively rated as “very good” or “excellent” by 50% of subjects on indiplon-MR vs. 17% of subjects on placebo. Indiplon was found to be safe, with no treatment-emergent changes in ECG or laboratory values.

Conclusions: In patients with mild-to-moderate COPD, indiplon was well-tolerated, and had no clinically significant effects on respiratory function as assessed by SaO2 and RDI.

References:


NR842 Thursday, May 6, 12:00 p.m.-2:00 p.m.
Cortical and Subcortical FDG Uptake in Never-Medicated Patients With Schizophrenia
Supported by Janssen Pharmaceutica and Research Foundation

Douglas S. Lehrer, M.D., Department of Psychiatry, Wright State University, 3533 Southern Boulevard, Suite 5200, Kettering, OH 45429, Monte S. Buchsbaum, M.D., Brad T. Christian, Ph.D., Joseph Mantil, M.D., Aaron Murray, B.A., Terry Oakes, Ph.D., Martin Satter, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to describe abnormalities in cortical and subcortical activation in medication-naive schizophrenic subjects using 18F-fluorodeoxyglucose PET imaging.

Summary:

Introduction: The prefrontal cortex and association nuclei of the thalamus work together in the modulation of attention, a prominent psychological deficit in schizophrenia.

Methods: We obtained position emission tomography with 18F-fluorodeoxyglucose on 12 never previously medicated patients with schizophrenia (seven men, five women, mean age 29.0) and 13 age- and sex-matched normal volunteers (eight men and five women, mean age 28.5) together with coregistered anatomical MRI. Patients were recruited from community referral in the Dayton, Ohio, area. During FDG uptake all subjects performed a spatial object identification attention task previously demonstrated to activate the thalamus in the region of the pulvinar. The task required identifying the letter “O” when surrounded by a visual field cluttered with flanking letters. FDG images were coregistered to the standard Montreal-Neurolological Institute brain and significance probability mapping carried out.

Results: Patients with schizophrenia had significantly lower relative metabolic rates in the prefrontal cortex, striatum, and thalamus.

Conclusions: Dysfunction of the fronto-striato-thalamic pathway is implicated in schizophrenia and the finding in never-previously medicated patients indicates that the relative reduction in metabolism is not due to the chronic or acute use of psychoactive medications.
the thalamus (p value for the thalamus=0.005, uncorrected) with 2
-type receptor PET to describe the binding of a high-affinity D
sen Pharmaceutica. way dysregulation.

volunteers (9 men and 6 women, mean age 27.4) with F-fally-
women, mean age 28.5) and 15 age- and sex-matched normal

Summary:

schizophrenic subjects, giving support to theories of schizophrenia

pride and F-FDG PET imaging. Data was coregistered and stan-

previously medicated patients with schizophrenia (10 men, 5

areas of the brain outside the striatum can be assessed.

F-Fallypride, 18
sen Pharmaceutica.

References:

Kettering Neuroscience Institute with additional support from Jans-

1. Hazlett EA, Buchsbaum MS, Byne W, Wei TC, Spiegel-Cohen
J, Geneve C, Kinderlehrer R, Haznedar MM, Shihabuddin L,
Siever LJ: Three-dimensional analysis with MRI and PET of the
size, shape, and function of the thalamus in the schizophrenia

2. LaBerge D, Buchsbaum MS: PET measurements of pulvinar

NR843 Thursday, May 6, 12:00 p.m.-2:00 p.m.
F-Fallypride Binding in Never-Medicated Patients With Schizophrenia
Supported by Janssen Pharmaceutica and Research Foundation

Monte S. Buchsbaum, M.D., Department of Psychiatry, Mt.
Sinai Medical Center, One Gustave Levy Place, Box 1230,
New York, NY 10029; Brad T. Christian, Ph.D., Douglas S.
Lehrer, M.D., Bing Shi, Ph.D., T. K. Narayanan, Ph.D., Jogesh
Mukherjee, Ph.D., Joseph Mantil, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to
describe the binding of a high-affinity D2-type receptor PET
ligand in striatal and extrastriatal sites in medication-naive schizo-

phrenic subjects using PET imaging.

Summary:

Introduction: Dopamine D2 receptor imaging of the striatum in
schizophrenia has not yielded consistent findings of a dopamine
abnormality. With the new high-affinity PET ligand 18F-Fallypride,
areas of the brain outside the striatum can be assessed.

Methods: We performed 18F-Fallypride PET imaging on 15 never
previously medicated patients with schizophrenia (10 men, 5
women, mean age 28.5) and 15 age- and sex-matched normal
volunteers (9 men and 6 women, mean age 27.4) with 18F-Fally-
pride and 18F-FDG PET imaging. Data was coregistered and stan-
dardized to the Montreal Neurological Institute brain.

Results: We observed significantly lower binding potential in the
thalamus (p value for the thalamus=0.005, uncorrected) with signif-
cance probability mapping as well as reduced FDG uptake in the
same region. These changes appeared most consistent in the
region of the medial dorsal nucleus. Tracing of the thalamic
cerebrocortical pathways is underway for a more precise local-
ization.

Conclusions: These findings suggest abnormal dopaminergic
modulation of thalamic association nuclei in medication-naive
schizophrenic subjects, giving support to theories of schizophrenia
related to dopamine dysfunction and fronto striato-thalamic path-
way dysregulation.

Funding Source: Takeda Pharmaceuticals North America, Inc.

References:

1. Goodnick PJ: Pharmacokinetics of second generation antide-

2. Stubbins CM, Karim A: A safety, tolerance, and pharmacokinetic
study of five single doses of TAK-375 in healthy adults. Sleep
2003; 26(suppl):A76.

NR845 Thursday, May 6, 12:00 p.m.-2:00 p.m.
Non-Nightly Zolpidem Use for Primary Insomnia Does Not Lead to Dose Increase
Supported by Sanofi-Synthelabo, Inc.

Michael L. Perlis, Ph.D., Psychiatry Department, Sleep
Research Lab, 300 Crittenden Boulevard, Rochester, NY
14642; W. Vaughn McCall, M.D., Andrew D. Krystal, M.D.,
James K. Walsh, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to
recognize that treatment of primary insomnia with zolpidem
taken on an “as needed” basis over three months did not result
in significant dose escalation versus placebo.

Summary:

Objective: Some evidence suggests that non-nightly use of hypno-
thetic medication does not result in dose escalation. The goal of
this investigation was to assess whether intermittent long-term zolpidem use was associated with escalating dosages.

**Methods:** 199 patients meeting the DSM IV criteria for primary insomnia were randomized to either zolpidem 10 mg or placebo for 12 weeks, in a double-blind, placebo-controlled trial. Participants were instructed to take at least three but no more than five pills per week. Medication use analysis was conducted using a 2 x 6 ANOVA. Variables for each ANOVA were Treatment (zolpidem vs placebo) and Time (baseline and six biweekly increments).

**Results:** Both treatments exhibited a nonsignificant trend toward dose escalation. Treatment by Time interaction was not significant (P<0.15), suggesting that the tendency to escalate the dose was not higher in either group. The placebo arm averaged one pill less per two-week interval. Patients receiving zolpidem averaged 8 pills during the first two weeks of the study period, gradually increasing that number by 0.4 pills.

**Conclusion:** Zolpidem can be maintained for sustained periods of non-nightly use, without significant concerns about dose escalation.

**Funding source:** Research supported by Sanofi-Synthelabo Pharmaceuticals.

**References:**

**NR846 Thursday, May 6, 12:00 p.m.-2:00 p.m.**
**Efficacy of Eszopiclone in the Treatment of Sleep-Maintenance Insomnia**
**Supported by Sepracor, Inc.**

Andrew D. Krystal, M.D., Department of Psychiatry, Duke University Medical Center, Room 54342 Trent Drive, PO Box 290, Durham, NC 27710, James Roach, M.D.

**Educational Objectives:**
At the conclusion of this presentation, the participant should be able to recognize the increased risk of psychopathology in children of parents with bipolar disorder as compared to children of non-mood-disordered parents.

**Summary:**
Objective: To compare the prevalence of psychiatric disorders among children who have a parent with bipolar disorder and children of non-mood-disordered parents.

Methods: 117 children of bipolar parents and 171 children of non-mood-disordered parents were evaluated using the Kiddie Schedule for Affective Disorders and Schizophrenia for children-Epidemiologic version (KSADS-E). Bipolar and non-mood-disordered parents of these children were also evaluated using structured interviews.

Results: Compared with children of non-mood-disordered parents, children of parents with bipolar disorder had elevated rates of depression (Odds Ratios [OR]=4.39, CI[2.39-8.05], p<.001), bipolar disorder (OR=13.85, CI[4.03-48.58], p<.001), GAD (OR=9.24, CI[1.15-74.33], p<.05), separation anxiety (OR=6.18, CI[2.52-15.14], p<.001), ADHD (OR=3.58, CI[1.56-7.70], p=.002), oppositional-defiant-disorder (OR=8.93, CI[3.66-21.77], p<.001), and substance abuse (OR=4.15, CI[1.02-16.81], p<.05).

Conclusions: Offspring of patients with bipolar disorder are at high risk for a range of psychiatric symptoms and disorders. Longitudinal studies are needed to clarify the relationship between psychiatric symptoms in early childhood and the subsequent development of bipolar disorder.

**Funding Source(s):** NARSAD and the Stanley Foundation

**References:**
Eszopiclone produced sustained objective and subjective improvements in sleep onset, sleep maintenance and total sleep time in adults with chronic insomnia, with no tolerance, rebound, withdrawal, or residual effects.

**Funding Source(s):** Sepracor Inc.

**References:**

**NR850**

**Thursday, May 6, 12:00 p.m.-2:00 p.m.**

**Four Studies of Eszopiclone Indicate Consistent Efficacy in Non-Elderly and Elderly Patients With Chronic Insomnia**

**Supported by Sepracor, Inc.**

Russell Rosenberg, Ph.D., Northside Hospital, 5780 Peach Tree-Dunwood Road, Atlanta, GA 30342; Robert Rubens

**Educational Objectives:**

At the conclusion of this presentation, the participant should be able to describe the objective and subjective effects of eszopiclone on sleep efficiency in elderly and non-elderly adult patients.

**Summary:**

**Objective:** Insomnia affects about 36% of adults and prevalence increases with age. Eszopiclone is a non-benzodiazepine under development to rapidly induce and maintain sleep in patients with insomnia.

**Methods:** Data are from randomized, double-blind, placebo-controlled studies of eszopiclone: two two-week studies of eszopiclone 2mg in elderly patients (PSG study, n=264, subjective study, n=160), and two non-elderly studies utilizing eszopiclone 3mg (6-week PSG study, n=204; six-month study, n=788). Each evaluated sleep onset, duration, and maintenance (wake after sleep onset—WASO).

**Results:** Eszopiclone significantly improved patient reports of sleep (onset, p<0.01; WASO, p<0.05; total sleep time, p<0.01) compared with placebo over the study period in elderly and non-elderly patients. In the two PSG studies, eszopiclone significantly improved sleep onset, sleep efficiency, and WASO in both populations (p<0.05). In all studies, eszopiclone patients reported improvements in measures of next day function.

**Conclusions:** These data demonstrate that eszopiclone provides consistent and reproducible improvements in patient-reported and PSG measures of sleep in non-elderly and elderly patients with chronic insomnia. Notably, consistent improvements in patient ratings of daytime functioning were also reported, indicating that eszopiclone may demonstrate efficacy in improving all four components of the DSM-IV diagnosis of primary insomnia in patients with chronic insomnia.

**Funding Source(s):** Sepracor Inc.

**References:**

**NR851 Thursday, May 6, 12:00 p.m.-2:00 p.m.**

**Disturbances of Endogenous Circadian Rhythms in Alzheimer’s Disease**

David Harper, Ph.D., Psychiatry Department, McLean Hospital, 115 Mill Street, Belmont, MA 02476; Ladislav Volcic, M.D., Edward G. Stopa, M.D., Mika Nitta, M.S., Andrew Satlin, M.D.

**Educational Objectives:**

At the conclusion of this session, the participant should be able to demonstrate the circadian contributions to sleep disturbance in Alzheimer’s disease.

**Summary:**

*Introduction:* One of the most disruptive symptoms of Alzheimer’s disease (AD) is sleep disturbance, and its presence frequently precipitates institutional placement. We have previously observed circadian disturbances in patients with probable AD [1].

*Method:* We studied core body temperature and locomotor activity in eight young and seven elderly controls and seven patients with probable AD (NINCDS-ADRDA criteria) using a fully constant routine protocol that makes the most accurate assessment of the endogenous circadian rhythm in human subjects. Subjects initially had a 72-hour locomotor activity recording, which was followed immediately by a 40-hour constant routine of core body temperature and locomotor activity [2].

*Results:* Subjects with probable AD had significantly delayed endogenous circadian phase as assessed from core body temperature recordings with temperature minima as late as noon. Endogenous amplitude was reduced in both elderly and AD groups. Phase synchronization in AD showed an abnormal loss of synchronization between temperature and activity that was not related to loss of endogenous circadian amplitude.

*Conclusions:* These results suggest that circadian rhythm disturbances may play a role in driving sleep disturbances in Alzheimer’s disease.

**Funding Source(s):** R01-AG20654, R01-AG09301, P30-AG13646 and Dept. of Veterans Affairs

**References:**


**NR852 Thursday, May 6, 12:00 p.m.-2:00 p.m.**

**Auditory Event-Related Potentials and Psychological Changes During Sleep Deprivation**

Leen Kim, M.D., Psychiatry Department, Korea University Hospital, Anam-Dong 5-Ga, Sungbuk-Ku, Seoul 136-705, Korea; Heon-Jeong Lee, M.D., Rhee-Hun Kang, M.D., Yong-Ku Kim, M.D., Kwang-Yoon Suh, M.D.

**Educational Objectives:**

At the conclusion of this session, the participant should know the effect of sleep deprivation on auditory event-related potentials.

**Summary:**

This study investigated the psychophysiological effects of sleep deprivation on auditory event-related potentials (AERPs) and their relationship with psychological parameters. Twenty-four subjects remained awake for hours under continuous surveillance. In the mornings and the evenings of two consecutive study days, AERPs were recorded and four self-rated scales (sleepiness, anxiety, mood) were quantified. The latencies of P300 and N200 were significantly prolonged (p<0.001) and their amplitudes decreased (p<0.05) as a consequence of sleep deprivation. However, the only significant change in N100 and P200 was an increase in the P200 amplitude (p<0.05). The increase in the latencies of P300 and N200 were correlated with increased sleepiness (p<0.05), and the increase in P200 amplitude was correlated with negative mood, anxiety, and fatigue (p<0.05). Although the changes in P300 and N200 induced by sleep deprivation are due to the sleepiness which may slow cognitive processing and decrease the efficiency of mental processing, the increase in P200 may be related with increased anxiety, negative mood, and fatigue.

**References:**


**NR853 Thursday, May 6, 12:00 p.m.-2:00 p.m.**

**Comorbid Substance Use Disorders in BDD**

Katharine A. Phillips, M.D., Department of Psychiatry, Butler Hospital/Brown University, 335 Blackstone Boulevard, Providence, RI 02906; Jon F. Grant, M.D., Maria Pagano, Ph.D., Christina Fay, B.A., William Menard, B.A.

**Educational Objectives:**

At the conclusion of this presentation, the participant will be familiar with results from the first study of the clinical correlates of substance use disorders in individuals with body dysmorphic disorder.

**Summary:**

*Background:* Little is known about substance use disorders (SUDs) in body dysmorphic disorder (BDD). The few studies of this topic found varying comorbidity rates, and none examined clinical correlates of SUD comorbidity.

*Methods:* We examined rates and clinical correlates of comorbid SUDs in 166 subjects with current DSM-IV BDD (69.9% female, mean age±32.5 ± 12.1) participating in a study of the course of BDD. The SCID and other reliable and valid measures were used.

*Results:* 48.8% of BDD subjects had a lifetime (i.e., current or past) DSM-IV SUD, and 21.7% had a current SUD. 42.8% had lifetime (and 13.3% had current) alcohol abuse or dependence; 33.7% had lifetime (and 14.5% had current) drug abuse or dependence 69.7% of subjects with an SUD reported that BDD contributed to the SUD: in 28.8%, BDD was the main or major reason for substance use; in 33.3%, BDD was somewhat of a reason; and in 7.6%, it was a minor reason. The mean age of SUD onset was 17.9 ± 5.9 compared with 15.4 ± 6.5 for BDD onset. SUD rates were similar in subjects who were and were not currently receiving mental health treatment (50.5% vs 45.6%). Males were more likely than females to have a lifetime SUD (62.0% vs 43.1%, p=.025). Compared to subjects without an SUD, those with a lifetime SUD had more severe BDD (p=.036) and more delusional appearance-related beliefs (p=.030). They also had a higher rate of suicide attempts (38.3% vs 17.7%, p=.003), history of inpatient hospitalization (43.2% vs 18.8%, p=.0007), and poorer functioning and quality of life as assessed by the SAS (p=.002), LIFE-RIFT (p=.014), SF-36 role limitations due to emotional problems (p=.014), and Q-LES-Q at a trend level (p=.057).
functioning.

Assessments were conducted at baseline, three months after random assignment to one of two treatment conditions, either 10 weekly sessions of cognitive behavior therapy (CBT) plus standard medical care (SMC) or SMC alone. Significantly more patients in the CBT plus SMC than in the SMC alone condition experienced significantly greater improvements in somatization symptom diaries, was the primary outcome measure. Additional assessments were conducted at baseline (i.e., posttreatment), nine months after baseline, and 15 months after baseline. Severity of somatization, as measured by symptom diaries, was the primary outcome measure. Additional measures were clinician-rated somatization severity and physical functioning.

Results: Intention-to-treat repeated measures ANOVA revealed significantly greater improvement in somatization severity and physical functioning than did patients receiving SMC alone (all p's < .05). Significantly more patients in the CBT plus SMC than in the SMC alone condition were rated by clinicians, blind to treatment condition, as "much improved."

Conclusion: CBT may produce enduring and clinically meaningful reductions in the discomfort and disability of patients with somatization disorder.

Funding Source(s): National Institute of Mental Health

References:


NR855 Thursday, May 6, 12:00 p.m.-2:00 p.m.
Psychological Impact and Coping Strategies of SARS-Team Nurses in Taiwan

Shwu-Hua Lee, M.D., Psychiatry Department, Chan Gung Memorial Hospital, 5, Fu-Shing Road, Kuei-San, Tao-Yuan, Taiwan; Yi-Jen Su, M.S., Yeong-Yuh Juang, M.D., Yi-Hui Lin, M.S., Hsin-Lan Lee, M.D., Chia-Chen Chao, Ph.D.

Educational Objectives:

The SARS team leader's recognition of staff's reaction is crucial for implementing psychiatric interventions to face the threatening of SARS outbreak. We demonstrate psychiatry can actively coordinate with the team work to help the staff and the hospital command center.

Summary:

Background: The outbreak of severe acute respiratory syndrome (SARS) in Taiwan began in April 2003. In our hospital, a nurse SARS-team of ED was established to manage this frightening situation. This study is to describe psychological impacts and coping strategies response to SARS among ED SARS-team nurses and the helpfulness of psychiatric intervention.

Methods: This study was conducted on the SARS-team nurses of ED in a general hospital in Taiwan. We delivered two debriefing groups, then identified important themes addressed by nurses. In-depth, semi-structured interview under audiotaped were performed. We reviewed tapes and composed a questionnaire.

Result: The SARS-team enrolled thirty nurses, 21 subjects (70%) attended the interview, 26 subjects (86.6%) completed the questionnaire. The result revealed worry about infecting families and colleagues, changing infection control procedures, and uncertainty were major stressors. The effective responses of reducing stress included psychiatric services, encouragement among peers, and enough rest. Nurses reported their own coping strategies practices personal protection measures and active learning the disease were helpful.

Conclusion: Our experience illustrates the leader's recognizing the staff's reaction is crucial for implementing psychiatric interventions to face the threatening condition. We highlight psychiatry should actively coordinate with the team work to help health-care workers.

References:


NR856 Thursday, May 6, 12:00 p.m.-2:00 p.m.
Hepatitis-C in a Large Cohort of Veterans: Rates of Screening and Testing

Eric W. Dieperink, M.D., Department of Psychiatry, Veterans Affairs, 1 Veterans Drive, 116A, Minneapolis, MN 55417; Paul Thuras, Ph.D., Samuel B. Ho, M.D., Mark L. Willenbring, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the prevalence of hepatitis C in various clinic populations.

Summary:

Introduction: Hepatitis C virus (HCV) infection disproportionately affects patients with mental health and substance use disorders
The Veterans Health Administration recommends that all patients be screened for hepatitis C risk factors and positive screens be tested for the virus. This study examined rates of screening and testing in a large health care system.

Methods: Medical chart data, abstracted by the VA’s Office Of Quality And Performance external peer review process (EPRP) from fiscal year 2002, were examined.

Results: Charts of 69,227 patients were reviewed. Within this cohort, 3,869 patients (5.6%) were found to have ever had a positive HCV antibody test. Positive HCV antibodies were more likely in patients treated for SUD 22.8% (941/4,123) or in patients with severe mental illness 16.6% (634/3,821). In patients identified as having a HCV risk factor by chart review, 80.3% (4,437/5,528) were clinically screened. However, screening for HCV was more likely in primary care 89.4% (2800/3134) than in mental health clinics 64% (1,265/1964) and lowest in SUD clinics, 56% (320/571).

Conclusion: HCV is most common in patients with SUD or severe and persistent mental illness, yet these groups have low rates of HCV screening. Systematic screening and testing initiatives are necessary in SUD and mental health clinics.

Funding Source: Supported by the VA Research Service and the Hepatitis C Resource Centers

References:


NR857 Thursday, May 6, 12:00 p.m.-2:00 p.m.
Suicidal Ideation During Interferon Treatment of Patients With Hepatitis-C
Eric W. Dieperink, M.D., Department of Psychiatry, Veterans Affairs, 1 Veterans Drive, 116A, Minneapolis, MN 55417; Samuel B. Ho, M.D., Lori Tetrick, Paul Thuras, Ph.D., Mark L. Willenbring, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize the risk of suicidal ideation in hepatitis C patients treated with antiviral therapies.

Summary:
Introduction/Objective: Psychiatric and substance use disorders affect most patients with chronic hepatitis C and are the most common reasons for exclusion from antiviral therapies. Suicidal ideation (SI) is often cited as a reason to exclude patients from interferon-based treatment or to terminate antiviral treatment that is in progress. This study examines SI in hepatitis C patients untreated and treated with interferon-α2b, a medication commonly associated with depression.

Methods: Hepatitis C patients eligible for treatment with interferon-α2b and ribavirin were recruited for the study. Measures of depression were administered at baseline and at 4, 8, 12, and 24 weeks of treatment.

Results: A total of 15/55 (27%) subjects reported SI while not on interferon therapy. Of the 42 patients treated with interferon, 18 (43%) endorsed SI at some point during antiviral treatment. However, 17/18 (94%) finished at least a six-month course of interferon therapy. No subjects attempted suicide.

Conclusions: Suicidal ideation is common in hepatitis C patients before and during interferon therapy. With adequate support, most patients can successfully complete a full course of interferon. Suicidal ideation should not limit patients’ access to care but close collaboration between hepatitis C practitioners and psychiatrists is indicated.

Funding Source: Unrestricted grant from Schering-Plough

References:


NR858 Thursday, May 6, 12:00 p.m.-2:00 p.m.
Helplessness Predicts Hypertension in Older Mexican and European Americans
Stephen L. Stern, M.D., Department of Psychiatry, University of TX Health Science Center, 7703 Floyd Curl Drive, MC7792, San Antonio, TX 78229-3900; Helen P. Hazuda, Ph.D., Rahul Dhanda, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to understand the possible relationship between helplessness and hypertension in older adults.

Summary:
Introduction: Our goal was to explore whether individual depressive symptoms might predict incident hypertension (HTN) in a cohort of 240 initially normotensive Mexican-American (MA) and European-American elders.

Methods: Subjects were aged 64–78 years on entering the San Antonio Longitudinal Study of Aging, an epidemiologic survey, in 1992–96. MA’s comprised 52% of the sample. On study entry all subjects completed the Geriatric Depression Scale (GDS) in English or Spanish. Their blood pressure was reassessed in 2000–01. Responses to six key GDS items (depressed mood, decreased interest, worthlessness, hopelessness, helplessness, and fatigue) were evaluated for the ability to predict HTN.

Results: In a univariate analysis, only helplessness significantly predicted HTN (chi-square=13.5, df=1, p<0.0003). In a Cox proportional hazards model adjusted for sex, education, number of comorbid diseases, current drinking, social well-being, and marital status, helplessness remained a very strong predictor (HR 4.99, CI 1.90–13.12, p=0.0011). Total GDS score, but none of the other individual items, also predicted HTN (HR 1.08, CI 1.00–1.17, p=0.0339).

Conclusion: Our findings suggest that helplessness may predict the development of hypertension in the elderly. Further research into this relationship and its mechanisms might help us to reduce our older patients’ risk for heart disease, stroke, and dementia.

Funding Source(s): This research was supported by NIA grant 5 RO1 AG16518-04.

References:


NR859 Thursday, May 6, 12:00 p.m.-2:00 p.m.
Depression and Acute Coronary Syndrome: Significance for Survival
Claus H. Sorensen, M.D., The Medical Research Unit, Amtsradhuset Torvet 7, Ringkobing DK-6850, Denmark; Erik F. Hasche, M.D., Torben Haghfelt, M.D., Per Bech, M.D.
Summary:

Introduction: Previous studies indicate that 15–20% of patients with acute coronary syndrome have a depression at discharge and that depressed patients may have an increased mortality during follow-up. Non-diagnostic questionnaires have often been applied.

Material and Methods: 899 patients admitted to 17 Danish hospitals with Acute Coronary Syndrome from March 1999 to December 2000 were included. At discharge, median day 7 after admission, the patients completed the Major Depression Inventory, an ICD-10 depression diagnostic questionnaire. For all patients relevant information was obtained from the hospital notes and from the National Death-Cause Register 12 months after discharge for information concerning death.

Results: In all, 10% had a depression at discharge. Women were more likely to be depressed than men, OR 2.5. There was no difference in relation to major cardiovascular risk factors, peak CK-mb value and ejection fraction between patients with and without depression at discharge. Depression at discharge was not related to 12 months mortality, OR 0.5.

Discussion: This is the largest study to use a validated depression diagnostic questionnaire. The prevalence of depression was lower than reported in other studies. Depression was not related to mortality, indicating that the use of non-diagnostic questionnaires may wrongfully associate depression with mortality after acute coronary syndrome.

Funding Source(s): Danish Heart Association

References:


NR860  Thursday, May 6, 12:00 p.m.-2:00 p.m.

Major Depression With Anger Attacks and Cardiovascular Risk Factors

Renerio Fraguas, Jr., M.D., Psychiatry Department, MA General Hospital, 50 Stanford Street, Suite 401, Boston, MA 02114; Dan V. Iosifescu, M.D., Bettina Bankier, M.D., Roy H. Perlis, M.D., Sarah Hamill, B.A., Cassandra Green, B.A., Maurizio Fava, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to evaluate the relevance of the association between anger/depression and cardiovascular risk factors.

Summary:

Objective: To investigate the association of anger attacks with cardiovascular risk factors among outpatients with major depressive disorder (MDD).

Methods: Three hundred drug-free subjects meeting DSM-III-R criteria for MDD, ages 18 to 65, were evaluated for the presence of major depression, anger attacks, and cardiovascular risk factors. A cumulated cardiovascular risk score (CRS, range = 0-6) was calculated following the NIH ATP III guidelines (based on the Framingham Heart Study) including age, gender, smoking status, family history, cholesterol, arterial hypertension, diabetes, and concomitant medication. The Anger Attacks Questionnaire (Fava et al. 1991) was used to evaluate the presence of anger attacks, and the 17-item Hamilton Depression Rating Scale was used to assess depression severity. Logistic regression was performed to assess the relationship between anger attacks and cardiovascular risk factors.

Results: Of 300 subjects, 127 (31.5%) met criteria for anger attacks. The CRS score significantly predicted the presence of anger attacks in a simple logistic regression analysis (p = 0.04, OR = 1.24, CI 1.009–1.538), and in a multiple logistic regression model (p = 0.002, OR = 1.51, 95% CI 1.157–1.986) that included BMI, male gender, age, and baseline Ham-D-17 scores. Anger attacks were present in 30 (37%) subjects of those with CRS score = 0, in 43 (40%) of those with SRS score = 1, in 29 (42%) of those with CRS score = 2, in 18 (54%) of those with CRS score = 3, in 6 (60%) of those with CRS score = 4, and in 1 (100%) subject with CRS = 5.

Conclusions: Total cardiovascular risk score was a significant predictor of anger attacks in subjects with MDD. Our data complements previous studies where anger and hostility were predictors of cardiovascular disease.

Funding Source(s): Presented by a Research Support from Conselho Nacional de Desenvolvimento Cientifico e Tecnologico-CNPG-Brazil

References:


NR861  Thursday, May 6, 12:00 p.m.-2:00 p.m.

Psychiatric Consultation for Somatoform Disorder in Primary Care

Christina M. Vanderfeltz-Cornelis, Ph.D., Department of Psychiatry, VU Medical Center, Valeriusplein G, Amsterdam 1075BG, Netherlands; Patricia Van Oppen, Ph.D., Herman Ader, Ph.D., Richard Van Dyk, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to give treatment advice to primary care practitioners of patients with somatoform disorder in primary care

Summary:

Objective: To evaluate the efficacy of a psychiatric consultation model for patients with somatoform disorder in primary care. These patients often resist psychiatric referral, suffer from concomitant anxiety or depressive disorders and disability, and burden health care with their high and inappropriate use of health care services.

Methods: Randomized controlled trial performed in primary care practices. 81 patients with serious somatoform disorder were selected and completed the study. 36 primary care practitioners (PCPs) cooperated. Psychiatric consultation (PC) by a psychiatrist in the presence of the PCP in the primary care practice setting was compared with care as usual (CAU) delivered by the PCP. Outcome measures were medically unexplained symptoms, mental symptoms, general and social functioning and level of health care utilization after 6 months.

Results: Analysis by a General Linear Model revealed that in the PC group all outcome measures improved significantly. Utilization of health care services diminished in the PC group but increased substantially in the CAU group.

Conclusions: Psychiatric consultation in the primary care setting is an effective intervention in the treatment of serious somatoform disorder. A further (cost-)effectiveness study is needed.

Funding: This study was performed with funding from the Dutch Ministry of Health Care.
The current study assessed Cloninger's Temperament and Character Inventory (TCI) and Costa & McCrae's NEO PI-R in 104 patients with MDD and 101 controls.

Results: An association was present between 5HTTLPR short allele/genotype, harm avoidance scores (p<0.05) and neuroticism (p=0.05) in patients with MDD only. This association was not present in the sample of non-psychiatric controls. Importantly, patients with MDD scored significantly higher in neuroticism (p<0.001) and harm avoidance (p<0.001) compared to the non-psychiatric controls.

Conclusions: Combined, these results support the proposal of a non-linear relationship between the 5HTTLPR alleles/genotypes and level of neuroticism/harm avoidance.

References:

NR864 Thursday, May 6, 12:00 p.m.-2:00 p.m.
Post-Concussive Symptoms in Mildly Head-Injured Litigants
Jim Andrikopoulos, Ph.D., Ruan Neurology, 1111 6th Avenue, West Building, Suite 400, Des Moines, IA 50314

Educational Objectives:
At the conclusion of this session, the participant should recognize non-improving, post-concussive symptoms in mild head-injured patients may reflect exaggeration of symptoms when seen in the context of litigation.

Summary:
Hypothesis: This study examined non-improving and/or worsening cognitive and physical post-concussive symptoms as a pre-
dictor of incompatible cognitive dysfunction in mild head injured litigants.

Methods: Mild head injured litigants (N=136) were asked about their post-concussive symptoms. Those with non-improving symptoms formed the high symptom group (HSG, n=58) and the remainder the low symptom group (LSG, n=78). The neuropsychological testing of a moderately to severely head injured inpatient group (CHIG, N=33) not in litigation was used as a control group.

Results: Patients in the HSG have a greater number of non-improving/worsening symptoms than the LSG (p<0.0001). The LSG has a greater number of impaired cognitive scores compared to the LSG (p<0.0001). The level of cognitive impairment in the HSG equaled that of a subset of the CHIG (85% of 33 patients; n=28).

Conclusions: Mild head injured litigants reporting non-improving or worsening post-concussive symptoms perform disproportionately worse on cognitive tests, indirectly suggesting exaggeration of post-concussive symptoms. The ideal control group would be a chronically symptomatic group of mild head injury patients who sustained a non-compensable injury (e.g., injury arising from a fall in the home where potential for litigation is improbable). During data collection, no such patient had been referred for testing.

References:

NR866 Thursday, May 6, 12:00 p.m.-2:00 p.m.
Maternal Infanticide: Data From 57 Mothers Hospitalized Forensically
Michael H. Stone, M.D., Department of Psychiatry, Columbia College of Psychiatry and Surgery, 225 Central Park West, Suite 114, New York, NY 10024-6027

Educational Objectives:
At the conclusion of this session, the participant should understand the dynamics and underlying factors behind maternal infanticide, the patterns according to maternal age, and possible preventive steps.

Summary:
Hypothesis: Mothers with severe mental illness who kill their children would not conform to the predictions from evolutionary psychiatry, according to which—women committing infanticide would be under age 25 (thus more able to replace a dead child) and would rarely kill a child past age one, when strong attachment already occurred.

Methods: All 57 cases of mothers admitted to the Mid-Hudson Forensic Hospital, 1974–2000, who had killed their own children were compared with the Canadian epidemiological data of Daly & Wilson (172 cases between 1974–1983), based on women who rarely showed severe mental illness. Demographic, clinical, and sociological variables were studied.

Results: The 57 mentally-ill MH mothers killed (or attempted to kill) 74 of their children. Their ages ranged from 16 to 54; μ-age was 30 (with SD=7.5 yrs). The child-victims ranged in age from 0 to 17 (μ = 3.81). In the Daly&Wilson sample, 76% of the mothers were under age 26 (134/172), 16 of the MH mothers were under age 26, x² = 47.06, p < 0.001. The mentally ill mothers were significantly more likely to kill a child older than 1 than were the mothers from the Daly&Wilson sample (x² = 20.1, p < 0.001).

Conclusions: Mentally-ill mothers (chiefly psychologically depressed or schizophrenic) who kill their children did not conform to evolutionary tenets, in that they often killed beyond the age when they could “replace” the lost child, and more often did so even when the children were of an age when normal mothers achieve maximal bonding.

References:

NR865 Thursday, May 6, 12:00 p.m.-2:00 p.m.
When Husbands Kill Wives: Personality and Social Factors Contributing to Uxoricide
Michael H. Stone, M.D., Department of Psychiatry, Columbia College of Psychiatry and Surgery, 225 Central Park West, Suite 114, New York, NY 10024-6027

Educational Objectives:
At the conclusion of this session, the participant should recognize the important factors that contribute to the risk of wife-killing (uxoricide) by husbands or other male sexual partners, and diagnose the personality disorders and attributes peculiar to this population.

Summary:
In previous epidemiological surveys of spousal murder by husbands (uxoricide) the personality patterns in the husbands (in some studies, other intimate male partners were also included) were characterized by “over-controlled” dependency: chiefly, passive-aggressive, avoidant, self-defeating and dependent. In one study, 31% of the uxoricide were followed by suicide of the husband. The murders usually involved “abandonment rage” and were carried out with “overkill” (viz., multiple stabbings). The few antisocial men killed “instrumentally”—often for insurance money. Demographic, clinical, and sociological variables were studied.

Results: The 57 mentally-ill MH mothers killed (or attempted to kill) 74 of their children. Their ages ranged from 16 to 54; μ-age was 30 (with SD=7.5 yrs). The child-victims ranged in age from 0 to 17 (μ = 3.81). In the Daly&Wilson sample, 76% of the mothers were under age 26 (134/172), 16 of the MH mothers were under age 26, x² = 47.06, p < 0.001. The mentally ill mothers were significantly more likely to kill a child older than 1 than were the mothers from the Daly&Wilson sample (x² = 20.1, p < 0.001).

Conclusions: Mentally-ill mothers (chiefly psychologically depressed or schizophrenic) who kill their children did not conform to evolutionary tenets, in that they often killed beyond the age when they could “replace” the lost child, and more often did so even when the children were of an age when normal mothers achieve maximal bonding.

References:
NR867  Thursday, May 6, 12:00 p.m.-2:00 p.m.  
Cerebrovascular Reactivity in Dementia of Alzheimer's Type Assessed by Acetazolamide Brain SPECT  
Dong Woo Lee, Department of Psychiatry, Sanggye Paik Hospital, Nowongu Sanggeddong, Seoul 137970, Korea; Jung Ho Lee, Maeng Je Cho, Jin Young Kim, Eun Jin Park, Jae Soo Sung, Sung Ju Kim  

Educational Objectives:  
At the conclusion of this session, the participant should be able to recognize the possible role of the abnormality of cerebrovascular reactivity in the pathophysiology of dementia of Alzheimer's type.  

Summary:  
Objectives: The purpose of this study was to investigate the abnormality of cerebrovascular reactivity in patients with dementia of Alzheimer's type by the acetazolamide brain SPECT, which has been used in the assessment of cerebrovascular diseases.  

Methods: Eighteen patients with dementia of Alzheimer's type, as diagnosed by the criteria of DSM-IV and NINCDS-ADRDA, and ten normal comparison subjects were recruited. They were rated by Mini-Mental Status Examination, Mattis Dementia Rating Scale, and Hamilton Depression Rating Scale. Acetazolamide brain SPECT scan of dementia patients and comparison subjects were analyzed by three-dimensional volume of interest method.  

Results: The results were as follows. There were significant differences in the values of cerebrovascular reactivity between the two groups. The cerebrovascular reactivity of dementia patients was significantly decreased in the right frontal lobes, and increased in left temporal lobe, compared to comparison subjects (p<0.05).  

Conclusion: There results imply the possible role of the abnormality of cerebrovascular reactivity in the pathophysiology of dementia of Alzheimer's type.  

Funding Source(s): This study was supported by The General Fund of Seoul National University Hospital.  

References:  

NR868  Thursday, May 6, 12:00 p.m.-2:00 p.m.  
Impact of Interventions to Prevent Depression in the Elderly  
Martin G. Cole, M.D., Department of Psychiatry, St Mary's Hospital, 3830 Avenue Lacombe, Montreal, PQ H3T 1M5, Canada; Nandini Dendukuri, Ph.D.  

Educational Objectives:  
At the conclusion of this session, the participant should know the feasibility and effectiveness of interventions relevant to preventing the onset of depression in older community subjects.  

Summary:  
Objective: To determine the feasibility and effectiveness of interventions to prevent the onset of depression in older community subjects.  

Methods: MEDLINE, PsyClNFO and HealthStar were searched for potentially relevant articles published from January, 1966 to June, 2003, January 1974 to June 2003 and January 1975 to June 2003, respectively. The bibliographies of relevant articles were searched for additional references. Twelve studies met the following six inclusion criteria: original research, subjects aged 18 years or more, controlled trial of a brief intervention relevant to preventing the onset of depression in older community subjects, determination of depression status at least 12 months after enrolment, use of an acceptable definition of depression. To examine feasibility we calculated study completion and participation rates. To examine effectiveness we calculated absolute (ARR) and relative (RRR) risk reductions for depression.  

Results: Study completion rates were 46% to 100%, median 77%; participation rates were 29% to 100%, median 83%. ARRs were −17% to 45%, median 8%; RRRs were 0% to 71%, median 39%. The evidence of effectiveness was most convincing for cognitive-behavioral interventions to reduce negative thinking.  

Conclusion: Cognitive-behavioral interventions to reduce negative thinking appear to have potential to prevent the onset of depression in older community subjects.  

References:  
NR870 Thursday, May 6, 12:00 p.m.-2:00 p.m.
Prolactin-Elevating Antipsychotics and Fractures in Older Adults
Marios Adamou, KIHNS, University of Kent, Research and Development Building, Canterbury CT2 7PD, United Kingdom; Michael Kavjma, M.D., Tilia Mertens, M.D., Anthony Hale, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize that the choice of an antipsychotic according to its prolactin elevating profile will not reduce the likelihood of fractures in an older adult population.

Summary:
Introduction/Hypothesis: Fractures in elderly people are an important public health issue. We investigated whether the use of prolactin-elevating antipsychotics is associated with an increased likelihood of fractures compared with the use of prolactin-sparing antipsychotics.

Methods: We identified older adult inpatients on antipsychotics (age 68–90, sd=5.52) with fractures confirmed by an X-ray for a five-year period (1998–2002). We compared these with a random group of older adult inpatient on antipsychotics (age 65–97, SD=7.15) with no fractures, from the same population and period, using as variables age, gender, type of diagnosis, use of hypnotics, anxiolytics and antipsychotics (prolactin-elevating vs prolactinsparing).

Results: Using binary logistic regression among 38 patients with fractures and 214 patients with no fractures, only the use of anxiolyotics (weight coefficient=3.12, SE=0.57, X²=29.75, p<0.001, odds ratio=22.75, 95%CI=7.40 to 69.88) and hypnotics (weight coefficient =1.72, SE=0.57, X²=9.10, p=0.03 odds ratio=5.57, 95%CI=1.83 to 17.02) proved to be a significant predictors of fracture occurrence. Age, gender, type of diagnosis, and the use of hypnotics, anxiolytics, and prolactin-elevating vs prolactin-sparing antipsychotics did not predict the occurrence of fractures.

Conclusions: The use of prolactin elevating antipsychotics in the elderly population is not associated with the occurrence of fractures. In contrary, the use of anxiolytics and hypnotics increase the likelihood of fractures in this population.

References:

NR872 Thursday, May 6, 12:00 p.m.-2:00 p.m.
Functional and Behavioral Effects of Memantine in Alzheimer’s Disease
Supported by Forest Laboratories, Inc.
Pierre N. Tarot, M.D., Department of Psychiatry, University of Rochester, Monroe Hospital, 435 East Henrietta Road, Rochester, NY 14620, Christopher H. van Dyck, M.D., Frederick A. Schmitt, Ph.D., Stephen Graham, Ph.D., Jason T. Olin, Ph.D., James Jin, Ph.D., Jeffrey L. Cummings, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to understand the efficacy of memantine for the treatment of functional and behavioral disturbances in moderate to severe Alzheimer’s disease patients.

Summary:
AD is associated with cognitive deficits, functional decline and behavioral disturbances. Memantine is a low-affinity, uncompetitive NMDA receptor antagonist thought to block prolonged activation of the NMDA receptor hypothesized in AD pathology. Memantine was approved for the treatment of moderate-to-severe AD based on demonstrated efficacy in two trials. Data from one 24-week, double-blind, placebo-controlled trial was further analyzed to assess memantine’s functional and behavioral effects in moderate-to-severe AD patients stabilized on donepezil (N=395, ITT population).

Functional abilities were assessed using the modified 19-item Alzheimer’s Disease Cooperative Study-Activities of Daily Living Inventory (ADCS-ADL 19) scale and the BGP-Care-Dependency subscale. Behavioral symptoms were assessed using the Neuro-psychiatric Inventory (NPI).

Memantine-treated patients demonstrated significantly higher functional ability (ADCS-ADL19 or BGP-Care-Dependency) compared to placebo-treated patients (p=0.028, p=0.001, respectively). A by-item analysis of ADCS-ADL 19 revealed that abilities...
in grooming, being left alone, and watching television were statistically significant in favor of memantine. NPI total score favored memantine treatment over placebo (p=0.002). NPI domains demonstrating statistically significant improvement after 24 weeks in memantine-treated patients were agitation/aggression, irritability/lability, and appetite/eating.

Memantine treatment in combination with ongoing donepezil therapy is associated with less functional and behavioral deterioration in AD than with donepezil therapy alone.

Funding Source(s): Forest Laboratories, Inc.

References:

NR874 Thursday, May 6, 12:00 p.m.-2:00 p.m.
Improvement in Tardive Dyskinesia in Elderly Patients on Aripiprazole
Supported by Bristol-Meyers-Squibb
Melinda S. Lantz, M.D., Psychiatry Department, The Jewish House, 120 West 108th Street, New York, NY 10025; Eric N. Buchalter, D.O.

Educational Objectives:
At the conclusion of this session, the participant should be able to: (1) recognize and evaluate elderly patients at risk for tardive dyskinesia; (2) identify antipsychotic therapies for psychotic patients with tardive dyskinesia and effectively monitor outcomes.

Summary:
Objective: To evaluate outcome of treatment with aripiprazole in elderly patients with psychosis and severe tardive dyskinesia. To assess the effect of aripiprazole therapy on the severity of tardive dyskinesia symptoms over a six month period.

Method: Retrospective chart review of four elderly nursing home residents treated with aripiprazole for psychotic symptoms, who displayed significant tardive dyskinesia from prior neuroleptic therapy. Subjects were identified from the nursing home population of patients with AIMS scores indicating severe tardive dyskinesia and receiving treatment with antipsychotic agents.

Results: The patients ranged in age from 77 to 92 years. All had cognitive impairment (mean MMSE = 11, range 7–19). Two had a diagnosis of Alzheimer’s dementia with psychosis, one suffered from bipolar disorder and one had schizoaffective disorder. All had significant prior exposure to antipsychotic agents (mean # years = 5, range 3–17). AIMS scores at the start of aripiprazole therapy indicated severe tardive dyskinesia (mean = 19.75, range 18–22), with functional impairment. After six months of aripiprazole therapy (mean dose = 10 mg/day), AIMS scores were reduced by an average of 5.5 points, with two patients regaining the ability to self-feed.

Conclusions: In this small sample of elderly patients with severe tardive dyskinesia, the partial dopamine agonist aripiprazole was associated with significant improvement in movement disorder symptoms when used for the treatment of psychosis. This offers a potential treatment benefit to older patients with psychosis who suffer from tardive dyskinesia.

Funding Source(s): Bristol-Myers Squibb

References:

NR875 Thursday, May 6, 12:00 p.m.-2:00 p.m.
Response to Mood Stabilizers in Patients With Bipolar I Disorder
Supported by GlaxoSmithKline
Martha Sajatovic, M.D., Department of Psychiatry, University Hospital Cleveland, 11100 Euclid Avenue, MS 5080, Cleveland,
At the conclusion of this session, the participant should be able to demonstrate an understanding of the efficacy and tolerability profiles of lithium and lamotrigine in older patients with bipolar I disorder (55 years or older), as ascertained by two large, 18-month multicenter studies.

Summary:

Introduction: Efficacy and tolerability of mood stabilizers in older bipolar patients remains understudied.

Objective: To examine response to lamotrigine, lithium, and placebo in older bipolar I disorder patients who were enrolled with a current or recent depressed (GW605) or manic/hypomanic/mixed (GW606) mood episode in two recently completed large maintenance studies.

Methods: 588 currently or recently symptomatic bipolar I patients (DSM-IV) were randomized to 18 months of double-blind monotherapy with lamotrigine (100–400mg/day), lithium (0.8–1.1mEq/L) or placebo. Efficacy outcomes (time from randomization until intervention for an emerging manic/hypomanic/mixed or depressive episode) were examined in patients who were age 55 or older at the time of study entry.

Results: The study population included 97 patients meeting age criteria. In this subgroup, time to relapse was significantly prolonged following lamotrigine (median survival = 202 days) but not lithium (139 days) treatment compared with placebo (99 days). The frequency and type of adverse events on lamotrigine treatment were similar when comparing older patients with the general study population.

Conclusions: Lamotrigine may be a useful treatment option for older bipolar patients requiring long-term mood stabilizer treatment due to its favorable efficacy and safety profiles.

Funding Source(s): Research funded by GlaxoSmithKline

References:

NR876 Thursday, May 6, 12:00 p.m.-2:00 p.m.
ApoE4 Allele Influences Antidepressants’ Cognitive Effects in the Elderly
Supported by Organon Inc.

Ruth O’Hara, Ph.D., Psychiatry Department, Stanford University, 401 Quarry Road, C-305, Stanford, CA 94305; Steven B. Hollander, M.D., William Lapp, Ph.D., Lee Boyle, Ph.D., Heidi Rodrigues, Helena C. Kraemer, Ph.D., Alan F. Schatzberg, M.D.

Educational Objectives:
At the conclusion of this session, the participant will be able to describe how the ApoE4 allele impacts the effect of antidepressant treatment on cognitive function in late-life depression.

Summary:

Introduction: A recent investigation suggests that older depressed patients with the ApoE4 allele may respond quicker to mirtazapine than paroxetine. We investigated whether the ApoE4 allele impacts the effects of these antidepressant treatments on cognitive function.

Methods: A total of 255 clinically depressed, older patients were tested at baseline and again after eight weeks of treatment with paroxetine or mirtazapine. The cognitive battery included measures of global cognition (MMSE), visuospatial ability (BVRT), attention and inhibition response (Stroop), psychomotor speed (Finger Tapping), executive function ( Trails B) and delayed verbal recall. Multiple regression analyses examined the effects on cognition of treatment received, the ApoE4 allele and controlled for age, gender and education.

Results: Overall, no significant positive cognitive changes were observed following antidepressant treatment. However, we observed positive effects of antidepressant treatment on cognition in patients with the ApoE4 allele which depended on type of treatment. Patients with the ApoE4 allele treated with paroxetine declined on the measure of attention and inhibition, while patients with the ApoE4 allele treated with mirtazapine did not decline. Patients with the ApoE4 allele in both treatment groups exhibited improvement in executive function. Independent of ApoE4 allele status, both treatment groups exhibited a significant decline in performance on visuo-spatial ability, but the paroxetine group exhibited significantly greater decline on this measure.

Conclusions: These results suggest that older depressed patients with the ApoE4 allele experience some benefits on cognition of antidepressant medication and that treatment with mirtazapine is more protective of cognitive function, particularly in those patients with the ApoE4 allele.

References:

NR877 Thursday, May 6, 12:00 p.m.-2:00 p.m.
Long-Term Use of Lamotrigine for Bipolar Disorder in Patients Over 55 Years of Age
Supported by GlaxoSmithKline

David B. Marcotte, M.D., 210 Fairway Dr, Fayetteville, NC 28305-5512

Educational Objectives:
At the conclusion of this session, the participant should be able to characterize the long-term (>76 weeks) effect of lamotrigine in bipolar disorder in patients 55 years of age or older.

Summary:

Methods: A retrospective chart review was performed. Charts were retrospectively scored every three months. In addition information was also collected retrospectively on weight change, presence of key bipolar symptoms, side effects and concurrent medications.

Results: Twenty patients with an average age of 63 (55 to 90) years, met study criteria. Nineteen patients received lamotrigine for an average of 100 weeks (76–328). Following titration the mean daily dose of lamotrigine was 182 mg/day, with a minimum and a maximum dose of 25 mg and 400 mg, respectively. mean CGI score was 4.8 (SD 0.96) at study entry and at last observation a mean change of –2.85 (p<0.0001) was noted. Changes observed in six bipolar symptoms were significant (p<0.005). There were no significant changes in patient weight (p=0.6579). Side effects were minimal with headache and cognitive disturbances reported in three of 14 patients. Antidepressants and minor tranquilizers were the most common medications used concurrently.

Conclusion: Although controlled studies are needed, lamotrigine appears to be safe and effective in patients over 55 years of age for long-term use.

Funding Source(s): Research supported by GlaxoSmithKline

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References:

NR878 Thursday, May 6, 12:00 p.m.-2:00 p.m.
A 20-Year Prospective Study of Adult Children of Alzheimer’s Disease
Lissy F. Jarvik, M.D., Department of Psychiatry, UCLA NPI, 760 Westwood Plaza, Los Angeles, CA 90024; Tracy R. Harrison, M.D., Bill Steh Matsuyama, Ph.D., Pauline Yaralian Larson, Ph.D., Lori Holt Schaeffer, Ph.D., Asenath Larue, Ph.D., Natalie L. Rasgon, M.D.

Educational Objectives:
At the conclusion of this session, the participant will recognize that significant cognitive decline is nearly inevitable during middle age for most offspring who have: 1.) a parent with clinically diagnosed AD (T/F); 2.) a parent and one or more other relatives with clinically diagnosed AD (T/F); 3. a parent with autopsy confirmed AD (T/F)

Summary:
Objective: Examine neurocognitive changes, 20 years after initial testing in adult children of Alzheimer probands.

Methods: Participation of 89 families with probands diagnosed as “probable” or “definite” AD in the 1980s was solicited for our 20-year follow-up. 25 offspring of 17 families constituting a convenience sample selected by geographic proximity and availability completed re-evaluation. Participants (40% male), ages 50–82 years (M=61.5 +/- 8.8) gave informed consent, underwent psychiatric evaluation and neurocognitive testing. Test-retest intervals between initial and 2002 evaluations ranged from 16.85–22.64 years (M=19.98 +/-30); 96% of the 25 had at least one additional interim evaluation.

Results: Preliminary analyses indicate that only the WAIS subtest Digit Symbol declined significantly during the 20 years and, there were no significant differences between those with/without autopsy confirmation or positive/negative family histories. None had diagnosable dementia.

Conclusions: Initial results suggest that despite having a parent with AD, many adult children can live to middle age and beyond without exhibiting significant cognitive decline. However, these findings need to be replicated with the remaining 18 surviving offspring in the 17 families as well as the surviving previously evaluated adult children of the other 49 families (23 families no offspring previously evaluated).

Funding Source(s): Funded by Albert Parvin Foundation & Lon V. Smith Foundation

References:

NR879 Thursday, May 6, 12:00 p.m.-2:00 p.m.
Drug Sensitivity and Periventricular Hyperintensities in the Aging Brain
Ian A. Cook, M.D., Department of Psychiatry, UCLA NPI, 760 Westwood Plaza, Room 37-426, Los Angeles, CA 90024-1759; Andrew F. Leuchter, M.D., Melinda Morgan, Ph.D., Michelle Abrams, R.N., Laura Mickes, B.A., Barbara Siegman, B.A.

Educational Objectives:
At the conclusion of this session, the participant should be able to describe the importance of specific types of white matter damage in linking anticholinergic load to brain dysfunction.

Summary:
Objective: To examine the relationship between sensitivity of the aging brain to anticholinergic challenge and volumes of subclinical structural brain disease (SSBD) such as periventricular hyperintensities (PVH).

Method: Psychiatrically-healthy elders (>65 y.o.) from the community (n=8, mean age 70) underwent structural MRI, and had a qualitative EEG (QEEG) recording while receiving an intravenous bolus of scopolamine (0.03mg/kg). Transaxial MRI scans were obtained with a GE Signa 1.5T scanner (double-echo sequence TE 3000, TR1 16, TR2 80, 3mm continuous slices, 256x256 window). Segmentation was performed with the MRX system [2]. QEEG recordings were acquired with the QND System using 36 scalp electrodes (International 10–20 System), SR 256 samples/sec/channel (0.3-70 Hz passband), and ElectroCap electrode caps. Drug sensitivity was assessed as change in alpha relative power (pre-infusion baseline to 30 minutes post infusion).

Results: Volume of PVH was significantly correlated with decrease in alpha power (r=0.7, p<0.05), but other SSBD measures (central and cortical atrophy; deep white matter hyperintensities) showed no significant correlation.

Conclusions: In this pilot study, CNS sensitivity to a standardized anticholinergic infusion was related to volume of PVH, but not other SSBD types. PVH may link health risk factors with increased sensitivity to side effects in the elderly.

Funding Source(s): PHS/National Institute of Mental Health, K08 MH01483, Drug Sensitivity in Elderly Psychiatry Patients

References:

NR880 Thursday, May 6, 12:00 p.m.-2:00 p.m.
Absence of Risperidone-Related Increased Stroke Risk in Dementia Patients
Supported by Janssen Pharmaceutica and Research Foundation
Chris Kozma, Ph.D., University of South Carolina, 112 Fox Hollow Circle, West Columbia, SC 29170; Luella Engelhart, Stacey Long, M.S., Andrew Greenspan, M.D., Ramy A. Mahmoud, M.D., Onur Baser, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to understand that treatment with risperidone does not confer greater risk for stroke-related events than treatment with other types of antipsychotics or with benzodiazepines in the 90 days following initiation of treatment.

Summary:
Objective: To compare stroke-related cerebrovascular adverse event (CAE) rates in dementia patients (age ≥60) treated with...
risperidone (RIS), olanzapine (OLA), haloperidol (HAL), benzodiazepines (BZD), and acetylcholinesterase inhibitors (ACI).

Methods: Retrospective cohort study; Medicaid data, 1999–2001. Inclusion criteria: (1) Alzheimer’s Disease or (pre)senile organic psychotic diagnosis or (2) ACI prescription. Patients on initial use of RIS were compared to OLA, and HAL patients; additional comparators were BZD and ACI patients. Analysis included six months pre- and three months post-index date. Logistic regression evaluated post-index stroke risk; CAEs defined as inpatient acute cerebrovascular events. Models included medication exposure, age, prior stroke, prior hospital days, anti-clotting agent usage, hypertension, atrial fibrillation, atherosclerosis, and diabetes.

Results: 939 RIS, 484 OLA, 395 HAL, 2419 BZD and 8773 ACI patients were analyzed. No differences found between OLA (OR=1.23, p=0.76), HAL (OR=2.69, p=0.16), or BZD (OR=1.37, p=0.55) versus RIS (reference). ACI versus atypicals (reference) was directionally different (OR=0.24, p=0.001).

Conclusions: Results suggest risperidone is not associated with higher risk of CAEs compared to other antipsychotics or benzodiazepines in elderly dementia patients. Different stroke rates between atypical antipsychotic- and ACI-treated patients likely reflect disparities in indications and dementia severity, which is known to be associated with stroke risk.

Funding Source(s): Janssen Pharmaceutica Products, L.P.

References:

NR881 Thursday, May 6, 12:00 p.m.-2:00 p.m.
Clinical and Demographic Correlates of Suicide Ideation in Older Patients
A. Joyce Young, M.D., Duke University Medical Center, 114 Crosswood Drive, Durham, NC 27703; John L. Beyer, M.D., Maragatha Kuchibhatla, Ph.D., Frederick Cassidy, M.D., Ranga R. Krishnan, M.D.

Educational Objectives:
At the conclusion of this session, the participants should be able to assess for suicide ideation in the elderly.

Summary:
Objective: The elderly are the fastest growing population in the U.S. The risk of suicide in this population is twice that of teenagers. There is limited information on the presence of suicide ideation in this population. The study was conducted to better understand the clinical and phenomenological correlates of elderly patients with bipolar disorder who experience suicidal ideation.

Methods: A cross-sectional study of 49 older adults (ages 50–89) with bipolar disorder was done. Assessing their history of suicide ideation we used a bivariate analysis, to evaluate potential clinical and demographic characteristics that may be associated with suicidal ideation.

Results: 30 subjects (60%) reported a history of suicidal ideation. Positive correlates include being Caucasian (p=0.04), having prominent sleep difficulties in the depressed phase (p=0.008). Those with a history of suicidal ideation were younger (mean age 58) compared with elders without a history of suicidal ideation.

Conclusions: Risk factors for older adults include Caucasian race and sleep disruption during depression. This study supports the previous findings, and may assist clinicians in the assessment for suicidal ideation in the elderly.

This study was financially supported by NIMH grant: #SR01 MH50570-5.

References:
1. Lifton I, Ketti PA. Suicide Ideation and the choice of advance directive by elderly persons with affective disorder.
2. Ouwend MA. Suicide behavior in bipolar mood disorder.

NR882 Thursday, May 6, 12:00 p.m.-2:00 p.m.
The Mini Mental-State Examination as a Screening Tool for Depression in the Elderly
Luis Aguera-Ortiz, M.D., Department of Psychiatry, 12 de Octubre Hospital, Rafael Calvo 30, Madrid 28010, Spain; Silvia Fernandez, M.D.

Educational Objectives:
At the conclusion of this session, the participants should be able to consider the potential use of the Mini-Mental State Examination cognitive test in the screening for depression, analysing the possible depressive content of the sentence written by the patient.

Summary:
Objective: Depression has important links with dementia either as a risk factor or as a complication. Detection of Depression in elderly populations is not easy in non-psychiatric settings and is frequently overlooked if patients do not complain of depressive symptoms. The Mini-Mental State Examination test (MMSE) is very widely used in the screening of cognitive impairment in specialized and non-specialized settings and could also be used as a screening tool for depression.

Method: Analysis and categorization of the content of the sentence written in the “Write a sentence” item of the MMSE, looking for sentences with a “sad” or “depressive” content. Data from 197 patients (age>64) with MMSE test, Yessavage’s GDS-15 test and DSM-IV diagnosis, in a Psychogeriatric outpatient facility were analyzed.

Results: A very wide range of contents was found. If dementia was present, simple sentences, with no significant depressive content were written. Depressive patients write either sad or non-sad sentences, with no statistically differences. Conversely, openly depressive sentences correlate (p<0.05) with major depression diagnosis (but not dysthymia).

Conclusions: The MMSE can help to screen for major depression in elderly non-demented patients, with virtually little extra effort.

References:

NR883 Thursday, May 6, 12:00 p.m.-2:00 p.m.
Age and Medical Comorbid Conditions in Bipolar Affective Disorder
Howard H. Fenn, M.D., Geropsychiatry Departments, VAHCS Palo Alto MPD, 795 Willow Road, Building 348, Menlo Park, CA 94025; Mark S. Bauer, M.D., Dwight L. Evans, M.D., Lori L. Althshuler, M.D., William O. Willford, Ph.D., Amy Kilbourne, Ph.D., Thomas P. Beresford, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to list four possible explanations for the finding that subjective
ratings of mental function are not lower in older age groups in this study.

Summary:

Introduction: Neither prevalence rates of comorbid medical illnesses nor their impact on functioning in bipolar affective disorder have been investigated extensively.

Methods: We obtained baseline functioning and chart medical diagnoses in 330 bipolars at index hospitalization and for the prior ten years. We ascertained prevalence rates of medical conditions, and applied multivariate analysis to identify covariates of current physical and mental function across age groups.

Results: Physical Component Score (PCS) decreased with age F (5,311)=3.7, p=0.003; current medical burden, but not age, was a significant correlate. Mental Component Score (MCS) displayed a U-shaped relationship with age; older subjects had higher scores, even without controlling for physical co-morbidity. Age and current anxiety disorder, not current substance disorder, contributed to lower MCS ratings in younger age groups.

Conclusions: Subjective ratings of physical function decline with age, but correlate with medical co-morbidity rather than age per se. Subjective ratings of mental function are not lower in older age groups. Interpretations: (1) Bipolar patients "accommodate to" illness (2) Illness severity, or comorbidities, lessen with age (3) Cohort effect makes younger participants more likely to have psychiatric comorbidity that lowers MCS, (4) Individuals with greater psychiatric impairment are less likely represented as they age.

Funding Source(s): V.A.H.C.S.

References:

NR884 Thursday, May 6, 12:00 p.m.-2:00 p.m.
Using an Electronic Assistive Device to Improve Treatment Adherence

Stephanie Berns, Ph.D., Cenorr Department, Zucker Hillside Hospital, 75-59 263rd Street, Glen Oaks, NY 11004; Sara Davis-Conway, M.A., Judith Jaeger, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the potential for improvement in life functioning and treatment adherence in patients with schizophrenia with the use of an assistive device.

Summary:

Objective: Studies have shown that not attending scheduled outpatient psychiatric programs occurs frequently and adversely affects clinical course in severely mentally ill populations. Neurocognitive deficits are prevalent in schizophrenia, are related to functional disability and may interfere with ability to adhere to a prescribed program. We hypothesized that the use of an electronic assistive device (EAD) similar to a pager would compensate for neurocognitive deficits and improve program attendance.

Method: A multiple baseline, single-subject series design was employed with six schizophrenia patients enrolled in a day treatment program. Baseline attendance was monitored for one month, after which subjects were given the EAD (treatment phase). For one month, subjects were paged with messages prompting them to wake up, leave for program, and to attend scheduled groups.

Results: Three of six subjects demonstrated significantly improved attendance for paged groups. Program absenteeism (non-attendance for whole day) also decreased significantly for two of the subjects. Relative to responders, non-responders had fewer neurocognitive deficits and their absences were readily explained by non-cognitive factors (i.e. program satisfaction).

Conclusion: Early findings suggest that EAD prosthesis may be effective only for those subjects having cognitive impairment. EADs offer a promising neurorehabilitative intervention for promoting treatment adherence in neurocognitively impaired psychiatric patients.

Funding Source(s): NARSAD funded

References:

NR885 Thursday, May 6, 12:00 p.m.-2:00 p.m.
Predictors of Psychiatry Resident Psychotherapy Competency

Kim A. Coon, Ed.D., Department of Psychiatry, University of Oklahoma, 4502 East 41st Street, Tulsa, OK 74135; William R. Yates, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to: (1) recognize at least three predictor variables of psychiatry resident psychotherapy competency; (2) describe the influence of competency prediction upon psychiatry training programs selection and training of residents.

Summary:

Objective: The objective of the study was to identify predictors of psychotherapy competence.

Method: Two psychiatry faculty blind to predictor variables independently ranked 21 residents for global psychotherapy competency. Minor ranking discrepancies were resolved by consensus. The rank order list was compared to a series of predictors that included sociodemographic, cognitive, and behavioral variables using rank order correlations. Discriminant function analysis was used to contrast groups with high and low competency ratings.

Results: Significant correlations between psychotherapy competency rank order were found for the following predictor variables: resident age (r = .61; p = .02); PGY-1 neurology global score (r = .65, p = .04); live psychotherapy supervision (r = .57, p = .03); USMLE Step 1 three-digit score (r = .80, p = .03); and Step 2 three-digit score (r = .70, p = .02). PRITE scores were identified as strong discriminants of psychotherapy competence in this sample. The discriminant function for PRITE scores for years one, two, three and four was 100%, 90%, 100% and 100% accurate respectively.

Conclusion: This study suggests that cognitive performance in the USMLE and PRITE tests correlates highly with faculty ratings of psychotherapy competency. Results from this analysis will require replication due to the limited sample size. Identifying predictors of psychotherapy competence may provide residency-training programs with direction in selecting resident candidates most likely to achieve competency and may allow training programs to focus limited resources on current residents who will benefit from enhanced training.
Characterization of Bias in the Last-Observation-Carried-Forward Method for Imputing Missing Data

Rebecca G. Knapp, Ph.D., Biometry and Epid Department, Medical University of South Carolina, 171 Ashley Avenue, PO Box 250835, Charleston, SC 29425; Yoku Y. Palesch, Ph.D., Renee Hebert, Ph.D., Wenle Zhao, Ph.D., Martina Mueller, Ph.D., Eunsil Yim, M.S., Charles H. Kellner, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to describe the importance of the amount of missing data and the time point at which the missing data occurs on magnitude of bias produced by the LOCF method for imputing missing data.

Summary:

Objective: To characterize, through a simulation study, the bias in estimating endpoint values resulting from the last-observation-carried-forward (LOCF) method for imputing missing data.

Methods: Using real data from a psychiatry clinical trial, we simulated data loss at different time points and for 5–45% amounts of loss. The difference between the "true mean" HAMD using complete data set and the mean of the simulated data sets was used as a measure of LOCF effect (bias). The probability of bias

References:

NR888
Thursday, May 6, 12:00 p.m.-2:00 p.m.
Characterization of Bias in the Last-Observation-Carried-Forward Method for Imputing Missing Data

Rebecca G. Knapp, Ph.D., Biometry and Epid Department, Medical University of South Carolina, 171 Ashley Avenue, PO Box 250835, Charleston, SC 29425; Yoku Y. Palesch, Ph.D., Renee Hebert, Ph.D., Wenle Zhao, Ph.D., Martina Mueller, Ph.D., Eunsil Yim, M.S., Charles H. Kellner, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to describe the importance of the amount of missing data and the time point at which the missing data occurs on magnitude of bias produced by the LOCF method for imputing missing data.

Summary:

Objective: To characterize, through a simulation study, the bias in estimating endpoint values resulting from the last-observation-carried-forward (LOCF) method for imputing missing data.

Methods: Using real data from a psychiatry clinical trial, we simulated data loss at different time points and for 5–45% amounts of loss. The difference between the "true mean" HAMD using complete data set and the mean of the simulated data sets was used as a measure of LOCF effect (bias). The probability of bias

References:
of a given magnitude for different amounts of missingness was determined.

Results: Bias increased as the amount of missing data increased, ranging from near 0 when only 5% of data were missing and the missing occurred near the end of the treatment course to 7.1 when 45% of data were missing and the missing occurred early in the treatment course. The probability of bias of magnitude \( \geq 3 \) was approximately 0.12 when 20% of the data were missing and the missing occurred uniformly over time.

Conclusion: These results illustrate that the difference between the "true" measure of endpoint computed from complete data and that estimated using LOCF can be large and its impact may depend upon the time and amount of missing data.

Funding Source(s): NIMH grant # MH55495

References:

NR889 Thursday, May 6, 12:00 p.m.-2:00 p.m.
Pharmacological Difference Between Escitalopram and Citalopram

Thomas Cremers, M.D., Biomonitoring Department, Groningen University, Antonius Deusinglaan 1, Groningen, NL 9713AV, Netherlands; Bho Westerink, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to evaluate the effect of escitalopram and citalopram in enhancing serotonin in the rat ventral hippocampus.

Summary:
Introduction: Citalopram is a 1:1 mixture of R- and S-enantiomers (R-citalopram and escitalopram, respectively). Recent nonclinical and clinical studies suggest that escitalopram has superior therapeutic activity compared with citalopram at corresponding doses.

Methods: The current set of experiments was designed to evaluate whether the proposed superior efficacy of escitalopram originated from a differential efficacy of escitalopram and citalopram in modifying central serotonin levels. We investigated the effects of citalopram and its enantiomers on extracellular serotonin levels using intracerebral microdialysis in ventral hippocampus of freely moving rats.

Results: Both citalopram and escitalopram dose-dependently enhanced serotonin levels in ventral hippocampus. Citalopram (10micromol/kg, s.c.) enhanced extracellular serotonin levels about five-fold, whereas escitalopram (5micromol/kg, s.c. equivalent to the amount of citalopram in 10 micromol/kg citalopram) enhanced serotonin levels 7–8 fold. Combining escitalopram with the R-enantiomer significantly attenuated the serotonin-enhancing effect of escitalopram.

Conclusion: Escitalopram is more effective in enhancing central serotonin levels than citalopram due to the inhibitory properties of R-citalopram on the effect of escitalopram, in line with other studies. Although receptor-binding data reveal no prominent affinities of the R-enantiomer of citalopram, it clearly reduces the effectiveness of escitalopram in enhancing serotonergic neurotransmission.

References:

NR890 Thursday, May 6, 12:00 p.m.-2:00 p.m.
Executive Ability Predicts Competence to Give Informed Consent in Psychoses

Vivienne Howe, Psy.D., Clinical Research Department, MHRI, Locked Bag 11, Parkville Melbourne, VIC 3052, Australia; Kellie Foister, B.S.C., Amber Clayton, B.S.C., Kym Jenkins, M.B., Loane Skene, LL.M., David Copolov, M.B., Nicholas A. Keks, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize that neurocognitive factors, particularly those associated with executive functioning, are the largest determinant of competence; and understand the association between psychiatric symptoms and competence is not as large as may be assumed.

Summary:
Objective: To determine the neurocognitive predictors of competence to give informed consent in patients with psychosis.

Method: 43 patients (27 male, mean age = 39.02 years SD= 12.21 years) with a DSM-IV diagnosis of schizophrenia (N=18) schizoaffective disorder (N=14) and bipolar affective disorder (N=11) participated. A battery of neurocognitive tests measuring intelligence, memory, reading ability and executive function was completed. The current standard measurement tool, the MacArthur Treatment Competence Research Instrument (MTCRI) full version, determined competency. Symptoms were rated on the Positive and Negative Symptom Scale (PANSS) by the treating psychiatrist who was blind to test results.

Results: Stepwise regression was used to predict the three aspects of competency determined by the MTCRI: understanding treatment decisions, perception of disorder and thinking rationally about treatment from patient performance on the neurocognitive test battery. The only significant predictor of each measure of competency was the Wisconsin Card Sorting Test. Variables related to symptoms, intelligence, attention memory and reading ability were not significant.

Conclusions: The single best determinant of competency is not the extent or severity of symptoms, nor is it intelligence, attention or memory. Rather, it is the patient’s ability to think adaptively and flexibly, using skills of executive functioning.

References:

NR891 WITHDRAWN

NR892 Thursday, May 6, 12:00 p.m.-2:00 p.m.
A Computerized Neurocognitive Battery for Psychiatrists

C. Thomas Gualtieri, M.D., North Carolina Neuropsychiatry, 1829 E. Franklin Street, #400, Chapel Hill, NC 27514; Lynda Johnson, Ph.D., Kenneth Benedict, Ph.D.
NR893 Thursday, May 6, 12:00 p.m.-2:00 p.m.
Cinema as a Instrument for Teaching in Liaison Psychiatry

Eva Garnica, M.D., Psychiatry Department, La Paz Hospital, Paseo Castellana 261, Madrid 28046, Spain; Ruth Berdun, M.D., Fabiola Irissari, M.D., Ana Hospital, M.D., Elena Fernandez-Leon, M.D., Marta Ramirez, M.D., Ignacio Millan, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to remark the usefulness of cinema as an instrument to popularize psychiatry among clinical staff.

Summary:
Objectives: We use cinema as a teaching tool in liaison psychiatry. It helps us to attach an image to each mental illness, detailing its various stages: how it starts, how it develops, or how it can be treated. Cinema connects the spectator with the main movie character, and in this way, adds a more subjective and personal experience to theoretical psychiatric knowledge.

Methods: Films which reflected several psychiatric aspects, such as specific diagnosis, social or legal problems due to mental illnesses, etc. were shown to other doctors in a general hospital once a week, during a whole year. The main movie aspects in which we wanted to be focused on, were explained before the movie was shown, and this was followed by a discussion panel on some clinical aspects of the patient pathology involved featured in the movie.

Results: A wide spectrum of hospital personnel (doctors from other specialities and nurses and other hospital personnel) came to our weekly meetings. The various sessions allowed the audience to understand several aspects of psychiatry, and above all, to understand their patients, regardless of having previous mental illnesses. The majority of the questions asked revolved around psychopharmacology, diagnosis, and how to treat or deal with depressed patients, alcoholics, drug abusers.

Conclusions: Cinema can be used as an effective instrument to help other doctors to achieve a better understanding of psychiatry, to create an empathy with the patient and to eradicate the stigma associated with a wide range of mental illnesses. This stigma still exists among some of our colleagues in other medical specialties and among part of our society.

References:

NR894 Thursday, May 6, 12:00 p.m.-2:00 p.m.
Cinema and Psychiatry: Bidirectional Relationship Through Traumatic Events in New York City

Marta Ramirez, M.D., Paz University Hospital, Paseo Castellana 261, Madrid 28046, Spain; Fabiola Irissari, M.D., Ignacio Millan, M.D., Ruth Berdun, M.D., Marta Morales, M.D., Elena Fernandez-Leon, M.D., Ana Hospital, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to mark the importance of cinema as an useful information source to get to now society’s psychological states.

Summary:
Introduction: The purpose of this descriptive study is to explore how the filming industry, as a source of leisure and entertainment, may be reflecting the social response in NYC after 9/11, and to what extent the potential changes correlate to those studied in Psychiatry and Psychology.

Methodology: A total of 61 films were selected for this study. All the films were produced and first shown in NYC between 1999 and 2003, and their Directors were listed as residents of NYC, according to the Directors Guild of America (DGA). The data gathered about each film included genre, initial budget, box office earnings during the opening weekend, and the number of theaters showing the film at that time. The data was obtained from the imdb.us database and was analyzed using the spss v.12 program.

Results: Compared to previous years (99,00,01), the number of dramas, action films, documentaries, musicals, science-fiction and adventure films increased, whereas the number of comedies, romance and terror films decreased.

Discussion: The literature research conducted on the psychological effects of 9/11 shows an increase in depression symptoms, PTSD and substance abuse among contextual victims. We postulate that the increase in dramas and action films post 9/11 may be reflecting these symptoms, as well as the coping mechanisms most frequently described by catastrophe victims: expressive (emotional expression and social support)/drama and active (fight and action)/action.

References:


NR895 WITHDRAWN

NR896 Thursday, May 6, 12:00 p.m.-2:00 p.m. Prevalence and Correlates of Erectile Dysfunction and Depression in a U.S. Population-Based Sample: Results From the Male Attitudes Regarding Sexual Health (MARSH) Study Supported by Pfizer Inc.

Raymond C. Rosen, Ph.D., Department of Psychiatry, Robert Wood Johnson Medical Center, 671 Hoes Lane, Piscataway, NJ 08854; Noel Gendrano III, M.P.H., Dale B. Glasser, Ph.D., Suzanne L. West, Ph.D., Culley Carson III, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize that erectile dysfunction and depression are strongly associated in black and Hispanic men relative to white men and that this association is independent of socioeconomic status and education level.

Summary:

Introduction: The MARSH study is the first nationally representative prevalence study of erectile dysfunction (ED) in men aged ≥40 years. We estimated the age-specific prevalence of ED and depression, and examined the relation between ED, depression, and ethnicity, which have not yet been examined using MARSH data.

Methods: We obtained a nationally representative sample of non-Hispanic white, non-Hispanic black, and Hispanic men aged ≥40 years. Men were classified as having ED if they were “sometimes”/“never” able to get and keep an erection satisfactory for sexual intercourse. Depression was assessed using the CES-D. Results: 901 white, 596 black, and 676 Hispanic men were interviewed. Age-adjusted ED prevalence estimates were 21%, 26%, and 22%, respectively; age-adjusted depression estimates were 9%, 15%, and 17%. Using age, socioeconomic status (SES), and education as covariates, depression was strongly associated with ED for black (RR 3.3 [1.7, 4.3]) and Hispanic men (RR 4.9 [3.3, 6.0]) but not for white men (RR 1.1 [0.7, 1.6]). Similarly, the rates of depression in black and Hispanic men with ED were elevated significantly. These results were independent of SES and education level.

Conclusions: ED and depression are common. Strong associations between ED and depression in black and Hispanic men have not been reported to date. This association warrants further investigation.

Source of Funding: Pfizer Inc

References:


NR897 Thursday, May 6, 12:00 p.m.-2:00 p.m. Get Ready, Get Set, Get Mad: PDA Records of Family Challenges in ADHD Supported by Eli Lilly and Company

Barbara Henker, Ph.D., Psychology Department, University of California, Los Angeles, Box 156304, Los Angeles, CA 90095-1563; Carol K. Whalen, Ph.D., Larry D. Jamner, Ph.D., Cara Kiff, B.A., Sharon S. Ishikawa, Ph.D., Joshua N. Floro, B.A., Joe A. Johnston, M.D., Amy R. Perwien, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant will be able to identify stress triggers in the daily lives of children with ADHD and their families, and recognize the promise of a new assessment procedure: high density, real-time monitoring using electronic diaries.

Summary:

Objective: To identify daily stress triggers using electronic diary reports from parents and children with ADHD.

Method: Participants were 23 children diagnosed with ADHD and taking long-acting stimulants (61% boys, Mage 10.4) and 23 non-ADHD peers (61% boys, Mage 10.8). Children and parents provided an average of 94 electronic diary reports of behaviors, moods, and contexts over a one-week period.

Results: Preparatory (“getting ready”) activities proved the most problematic, despite occurring only 7% to 10% of the time. Compared to controls, parents of children with ADHD spent 50% more time getting their child ready, were 6 times as likely to report this task as difficult, and were 5 times as likely to report anger when getting child ready. Control, but not ADHD, children were almost twice as likely to report “getting ready” (compared with other activities) as something they were good at, yet both groups perceived this task as more difficult (ORs 2.88, 2.78) and reported more anger (ORs 3.63, 2.45) than during other activities.

Conclusion: Even when children with ADHD are receiving stimulant treatment, the preparatory tasks of daily living are especially challenging and linked disproportionately to parent negative affect and low self-perceived efficacy. Treatment targeted on these transitional hurdles may improve family harmony.

Funding Source(s): Funded by Eli Lilly and Company

References:


NR898 Thursday, May 6, 12:00 p.m.-2:00 p.m. Taking Medication Is a Sin: Nonadherence Due to Religion

S. Pirzada Sattar, M.D., Psychiatry Department, Creighton University, 4101 Woolworth Avenue, #116A, Omaha, NE 68105; Shakeel Ahmed, M.D., Sri ram Ramaswamy, M.D., Subhash Bhatia, M.D., Frederick Petty, M.D., Shruti Malik, M.H.A., Daniel R. Wilson, M.D.

Educational Objectives:

At the conclusion of this session, participants should be able to understand the ethical conflict of prescribing medications with ingredients forbidden by certain patient's religions.

Summary:

Objective: To survey physician and patient attitudes to prescribing medications which contain components forbidden by some patient's religious beliefs.

Method: In this pilot study we surveyed a random convenience sample of Psychiatrists and patients (N = 100 patients, 100 Psychiatrists) using a questionnaire approved by the Creighton University IRB
Results: Survey included 100 patients who agreed to complete our questionnaire, 63% said it was important for physicians to inform patients when medications contain Gelatin or stearic acid of Beef or Pork origin, as it may offend some patient's religious beliefs. Survey included 100 psychiatrists, of which 70% thought that it was important to inform patients about the possibility of their medication containing gelatin or stearic acid of beef or pork origin.

Conclusion: For some patients whose religious beliefs prevent them from ingesting pork or beef products, taking medications that contain these forbidden substances is a grave matter. According to the Physician Desk Reference more than 770 medications contain stearic acid and more than 330 medications contain gelatin of pork or beef origin. Therefore Psychiatrists, when prescribing medications to patients whose religions prohibit consumption of pork or beef products should inform their patients of this possibility.

References:

NR899 Thursday, May 6, 12:00 p.m.-2:00 p.m. 
Cinema and Psychiatry: Use of a Short Movie as a Complementary Tool in Teaching Theory of Grief
Fabiola Irisarri, M.D., Psychiatry Department, La Paz University Hospital, Paseo de la Castellana 261, Madrid 28046, Spain; Ruth Berdun, M.D., Elena Fernandez-Leon, M.D., Ana Hospital, M.D., Ignacio Millan, M.D., Marta Ramirez, M.D., Marta Morales, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to demonstrate the usefulness of the cinema-graphic support in teaching the theory of psychiatry to medical students.

Summary:
Hypothesis: We believe that cinema shares a bidirectional link with the spectator. It allows an objective approach to the story, so that it can be summarized, categorized, and referred to a theoretically described procedure (manual). An intersubjective relationship between the spectator and the movie character is settled due to an identifying procedure. Therefore, there is a bigger individualization, empathy is developed and a reflexive and critical glance is possible.

Methods: We produced and presented to medical students a short movie (24). Three siblings' different reactions when facing their father's death are shown. Common elements to grief reactions are subtitled. The program and a short description of Wodden's grief theory are previously exposed. Afterwards, we head for a short discussion and ask for the questionnaires to be fulfilled (1 hour in all). Each questionnaire is composed by nine items total: five multiple choice items and four open questions about the project. The open questions' answers are categorized as follows: difficulties in understanding grieving, emotional changes, thinking changes, theoretical learning.

Results: 98% answered correctly to multiple choice questions. 81% found the program more useful than a theory class. 52% changed previous attitude towards grief. 65% got to empathize with the characters.

Discussion: We believe that cinema can be a valuable complementary tool for Psychiatry learning and teaching. Our experience may be also applied to other liaison psychiatrists in other general hospitals.

References:
Educational Objectives:
At the conclusion of this session, the participant should be able to demonstrate understanding of methods that may be used to educate youth about mental illness, and demonstrate knowledge about the impact of mental illness on adolescents.

Summary:
Objective: To assess the effectiveness of a mental health educational intervention for high school students. The aim of the intervention is to increase knowledge and to change attitudes and behavior regarding mental illness.
Methods: High school students (N=756) attended a standardized, 60-minute mental health educational seminar. This intervention group completed pre- and post-questionnaires to assess knowledge, perceived stigma of mental illness, and help-seeking behavior. A control group (N=242, matched by school and grade level) completed the pre-questionnaire.
Results: After the seminar, students were statistically more likely to say “I know a lot about mental illness (P=0.00),” 75% vs. 44%. Students identified more mental illness in themselves (P=0.00), 25% vs. 16%, and 24% stated “Because of what I learned today, I may need help for a mental illness”. Students were more likely to know where to get help for mental illness (P=0.00), 80% vs. 46%. More students stated “Mental illnesses are treatable” (P=0.00), 86% vs. 60%.
Conclusion: Students demonstrate increased knowledge and positive change in attitude regarding mental illness after attending the presentation. Results support the benefit of mental health education in high school. Students will be surveyed at three months to measure the stability of change over time.

Funding Source(s): American Psychiatric Foundation

References:

NR902 Thursday, May 6, 12:00 p.m.-2:00 p.m.
Stigma of Mental Illness: A Survey of High School Students
Stephanie Riolo, M.D., Psychiatry Department, University of Michigan, 2101 Commonwealth, Suite C, Ann Arbor, MI 48105; Tuananh Nguyen, M.D., Cheryl King, Ph.D., Heather Irish, B.A., Sentra Faru, B.S.

Educational Objectives:
At the conclusion of this session, the participant should be able to demonstrate an understanding of stigma of mental illness among adolescents and identify factors that contribute to perceived stigma of mental illness.

Summary:
Objective: To measure adolescents’ beliefs about the stigma of mental illness, including perceived discrimination and need for secrecy. Results are compared by age, gender, race/ethnicity, grade-point average (GPA), and school demographics.
Methods: The Link Stigma Scale was used to survey 836 high school students in five Midwestern communities.
Results: Adolescent males are statistically more likely to keep mental illness a secret (p=0.03). There is no significant difference between males and females with respect to perceived discrimination against persons with mental illness. Perceived discrimination does not differ significantly by race/ethnicity or GPA; however, students are more/less likely to keep mental illness a secret depending on their school. Over 50% believe mental patients are less intelligent than average. Over 40% believe entering mental health treatment is a sign of personal failure. Forty-five percent would not accept a former mental patient as a friend. Only 35% of students would accept recovered mental health patients as teachers and less than 10% would hire them to care for their children.
Conclusion: The majority of high school students in the Midwest endorse discrimination against persons with mental illness. Gender is a strong factor in students’ readiness to disclose treatment for mental illness.

Funding Source(s): American Psychiatric Foundation

References:

NR903 Thursday, May 6, 12:00 p.m.-2:00 p.m.
Stigma By Proxy: Exploring Caregivers of Patients With Bipolar Illness
Stephanie Jaros, M.A., Department of Psychiatry, Stanford University, 401 Querry Road, Stanford, CA 94304-1419; Matthew Schumacher, M.A., Jennifer Culver, Ph.D., Andrea M. Alarcon, B.A., Natalie M. Baloga-Mintz, Deborah Derlick, Ph.D., Terence A. Ketter, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize self-stigma experienced by caregivers of bipolar patients and its relationship to psychosocial factors.

Summary:
Objective: To explore self-stigma by proxy among caregivers of patients with bipolar disorders.
Method: Caregivers (n=103, age=46.1 ± 11.6 years, 56% female, 85% Caucasian, 60% spouses/partners, 20% parents, 8% children, 7% siblings, 5% other) were interviewed for the Family Experience Study (FES) certified by the Systematic Treatment Enhancement Project for Bipolar Disorder (STEP-BD). Caregivers were assessed with a battery of psychosocial measures, including 11 items assessing self-stigma.
Results: Caregivers of female patients endorsed self-stigma items more strongly than caregivers of male patients (p<0.05) as did caregivers who did not live with patients (p<0.05). Similar endorsements related to: greater caregiver depression (average r=0.31, ps<0.01), greater sleep troubles (average r=0.23, ps<0.05), poorer relationships with patients (average r=0.28, ps<0.05), less patient appreciation for caregivers (r=-26, p<0.01), and younger patient age at first treatment (r=0.23, p<0.05) and hospitalization (r=-0.30, p<0.02). Additionally, caregivers who endorsed self-stigma items more strongly were more upset by patient criticism (r=0.23, p<0.05) and indicated that patients grew more upset when criticized (average r=0.22, ps<0.05).
Conclusion: Results indicated that caregiver self-stigma related to important psychosocial outcomes, warranting further research in this understudied area.

Funding Source(s): National Institute of Mental Health

References:

NR904 Thursday, May 6, 12:00 p.m.-2:00 p.m.
Prospective Data Acquisition in the Psychiatric Emergency Service (PES): Methodological and Validity Issues
Yves Chaput, M.D., Psychiatry Department, McGill University, Douglas Hospital, Reed Pavilion 6875 LaSalle Boulevard, Montreal, PQ H4H 1R3, Canada; Edith Labonte, M.D., Lucie Beaulieu, M.D., Marie-Josee Lebel, R.N., Michel Paradis, M.D.

Educational Objectives:
At the conclusion of this session, the participant should understand the pitfalls of generalizing from clinical data samples acquired without prior knowledge of the possible sources of error versus inserting data into a research database.

Summary:
Epidemiological data represent a cornerstone upon which modifications made to a clinical service rest. Acquiring data prospectively in a high pressure environment where time is often a limiting factor presents many challenges.

The objective of this study was to assess potential sources of variance (SV) for several clinical variables prior to their insertion into a prospective PES-based research database.

Methods: Clinical/demographic variables (of up to 70 variables/visit in a complete dataset) were acquired from patients visiting four major PESs (three metropolitan, one suburban/rural) in the province of Quebec during a 12-month period.

Results: Three potential SV were examined. First, the overall number (in %) of visits where datasets were not obtained was assessed and ranged from 8% to 17%, depending on the PES (10.4%, weighted average). This rate was independent of patient volume. Second, once a dataset was obtained, the overall % missing data rate for each variable within it was assessed. For example, history of substance abuse (SA) and family history of mental illness (FH) showed a 10% to 25% (14% weighted average) and an 11% to 21% (15% weighted average) missing data rate, respectively. Third, the ‘internal consistency’ of variables within the dataset was examined by determining the frequency with which a variable was tagged inconsistently during repeated visits by the same patient to the PES. Both SA and FH showed substantial inconsistency ranging from 12% to 16% (14% weighted average) and from 16% to 22% (weighted average of 18%), respectively.

Conclusion: These results suggest that although inferential statistics are important tools for the formulation and testing of clinical hypotheses their usefulness can be hampered by in the inclusion of unstable or incomplete variables prior to data analysis.

This work was supported in part by a grant from ‘Valorisation Recherche Quebec’.

References:

NR905 Thursday, May 6, 12:00 p.m.-2:00 p.m.
Racial and Ethnic Disparities in the Mental Health Care System
Chandresh Shah, M.D., Los Angeles Veterans Affairs Clinic, University of Southern California, 351 East Temple Street, # 116 A, Los Angeles, CA 90012

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize factors affecting racial and ethnic disparities in mental health care system.

Summary:
The report by the Surgeon General of the United States has identified culture, race, and ethnicity as variables in mental healthcare system. Patients’ access and providers’ biases have been noted as two significant issues leading to racial and ethnic disparities in health care. The first step in the interaction between a patient and a provider is an administrative process of patient assignment. To study racial and ethnic issues affecting this process, data was collected for patients enrolling into mental health clinic over a period of 12 months. There were 590 patients who were assigned to three different providers without each others’ identity. There were 2.71% Asian (A), 47.80% Black (B), 22.03% Hispanic (H) and 27.46% White (W) patients. Providers were categorized as Asian Indian (A-I), Far East Asian (A-E) and White (WW). After correction for equal distribution in assignments, the data show that 37.19% of W were assigned to WW in contrast to only 26.78% of them being assigned to A-I (p<0.001). In an opposite scenario, 37.18% of B were assigned to A-I as compared to 31.38% to WW and 31.44% to A-E (p<0.05). The assignments of A were numerically favored for WW, but did not reach statistical significance. No differences were noted in assignment of H to any other providers. These data illustrate that even non-patient, non-provider factor like administrative process plays a role in bringing racial and ethnic disparities in mental healthcare system.

References:

NR906 Thursday, May 6, 12:00 p.m.-2:00 p.m.
May Medically Assisted Procreation Be Relevant for Homosexual Women?
Jean-Michel Darves-Bornoz, M.D., Department de Psychiatrie, Hoipital General, 149 Boulevard Roosevelt, Vendome 41100, France; Regine Sintes, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to reflect on ethical problems.

Summary:
Certain voices in France require medically assisted procreation (MAP) for lesbians. Even though law did not allow such a possibility in France, it seemed interesting to question professionals actively involved in the use of MAP techniques.

Through systematic internet queries, we obtained a list of one hundred private or public French medical institutions with a MAP unit. A sample of 147 gynaecologists practicing MAP was then drawn. They answered to a clinical instrument with ended-questions in order to assess their opinions on: homosexual women with a desire of a child, possibility for these clinicians to intervene with a donor insemination in such situations; developmental risk for such children: 125 accepted to answer (85%).

Nine percent of these gynaecologists still consider homosexuality as pathological, and 10% as deviant and 5% deny any maternal abilities to homosexual women. Before the French laws of bioethics in 1994, none of them had practiced a donor insemination
for a lesbian couple, though 4% had realized some for single homosexual women. Two thirds of them do not agree opening donor insemination to homosexual women. 87% think that a child brought up by homosexual parents is at risk for developmental disorders. The supposedly most important risk factors are thought to be the marginality of an homosexual family and the lack of a paternal figure at home. However, for 68% of the clinicians, this role can be taken by another male figure. These reasons make the gynecologists reluctant to participate actively in the constitution of such a kind of family by the practice of a donor insemination. Even though demands of lesbian couples were not listed as an indication of donor insemination in the laws of bioethics, this does not seem to lessen the number of these demands in this population, and moreover if the law would allow this indication, half of these doctors would agree to practice it.

References:

NR907  Thursday, May 6, 12:00 p.m.-2:00 p.m.
Developing a Brief and Efficient Mental Health Screen for Jails
Julian Ford, Ph.D., Department of Psychiatry, University of Connecticut Health Center, 263 Farmington Avenue, Farmington, CT 06030; Robert L. Trestman, M.D., Valerie S. Hogan, M.A., Susan Quarti, M.A.

Educational Objectives:
At the conclusion of this session, participants will be able to describe the prevalence of mental illness in male and female jail populations, recognize the growing need for improved mental health screening tools, and understand constraints and processed involved.

Summary:
As of December 2002, there were an estimated 2,166,260 incarcerated in federal and state correctional facilities during the year. With prison populations growing at an average of 45,000 per year (since 1995) and the estimated number jail and prison inmates with mental illness ranging between 8% and 16% of total population, we anticipate over 350,000 inmates with past or current mental health concerns in the US correctional systems by the end of 2003. Timely identification and triaging of individuals with mental illness upon incarceration is a critical step in addressing public health and safety concerns associated with these individuals.

This presentation will discuss results from Phase I of a two-phase study that has developed an 8–12 item screen with versions designed to optimize sensitivity and specificity for predicting the presence of undetected psychiatric disorders in White, Black, and Latino men and women at incarceration. Results of discriminate function and receiver operator characteristics (ROC) analyses will be presented separately by race and gender for the prediction of undetected Axis I or II diagnoses. Overall predictive power of the screen ranged from 67% to 94% and cutpoints for different predictive threshold will be presented. Phase II, the cross-validation of the shortened screening tool (8-items for women and 12-items for men) begins in December 2003 and will be briefly overviewed.

Funding Source(s): National Institute of Justice (#200 IJ CX 0044)

References:


NR908  Thursday, May 6, 12:00 p.m.-2:00 p.m.
Mental Health and Chronic Pain: The National Comorbidity Survey Replication Supported by Pfizer Inc.
Paul Stang, Ph.D., Galt Associates Incorporated, 640 Sentry Parkway, Suite 305, Blue Bell, PA 19422; Ronald C. Kessler, Ph.D., Nancy Brandenburg, Ph.D., Michael Lane, Ph.D.

Educational Objectives:
At the conclusion of this presentation, participants should have improved understanding of the frequency of anxiety disorders among pain patients and the causal mediators between these disorders.

Summary:
Objective: To describe the relationship between chronic pain conditions and psychiatric disorders in the National Comorbidity Survey Replication (NCS-R).
Methods: NCS-R is a face-to-face survey of 9090 respondents, 18 and older, from a probability sample of the non-institutionalized US population fielded February, 2001-December, 2002. Psychiatric disorders were assessed using the Composite International Diagnostic Interview; medical conditions were ascertained through a Chronic Conditions Checklist.
Results: Over 7% of the population suffers from chronic pain not associated with arthritis, headaches, or back and neck problems ("other chronic pain" or "medically unexplained chronic pain"). Almost one third of those with other chronic pain or medically unexplained chronic pain had conditions often associated with neuropathic pain (i.e., diabetes, HIV, cancer, stroke). Retrospective age-of-onset reports suggest psychiatric disorders comorbid with pain conditions have an earlier age of onset than the pain conditions. Survival analyses suggest psychiatric disorders significantly predict onset and persistence of these pain conditions. Anxiety disorders were more important than mood disorders in predicting chronic pain onset and persistence.
Conclusions: Replication and extension of anxiety as an important predictor of pain is needed to address potential methodologic issues and to refine understanding of the causal mediators of psychiatric disorders and chronic pain.

Study funded by the National Institutes of Mental Health. Additional analyses funded by Pfizer.

References:

 NR909  Thursday, May 6, 12:00 p.m.-2:00 p.m.
Antipsychotics and Diabetes-Related Adverse Events: The FDA’s Adverse Event Reporting System (AVERS) Database
Supported by Janssen Pharmaceutica and Research Foundation
Krishnan Ramaswamy, Ph.D., Janssen Pharmaceutica, 1125 Trenton-Harbourton Road, Titusville, NJ 08560; David M. Fram,
B.S., Xionghu Yang, Ph.D., Ramy A. Mahmoud, M.D., Amy L. Grogg, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize spontaneous report data that suggest that antipsychotics may have different diabetes-related adverse-effect profiles, including life-threatening events.

Summary:

Objective: Diabetes-related adverse effects are an emerging concern with some antipsychotics, therefore metabolic risks associated with antipsychotics are compared.

Methods: Adverse Event Reporting System (AERS) data from 1968 through the third quarter of 2002 were combined yielding approximately 2.2 million reports. Adverse events studied included 15 MedDRA Primary Terms (MPTs). The agents studied were risperidone, olanzapine, quetiapine, clozapine, ziprasidone and haloperidol. An empirical Bayes data-mining algorithm was used to measure association strength. For each drug-event combination the Empirical Bayes Geometric Mean (EBGM) and 95% CI was calculated.

Results: Life-threatening events: Olanzapine had EBGM scores > 8 times expected for combined MPTs such as diabetic ketoacidosis and diabetic coma NOS. Diabetes: Olanzapine and clozapine had EBGM scores > 3 times and > 4 times expected for new onset diabetes MPTs combined. Abnormal Blood Glucose: Olanzapine had EBGM scores > 2 times expected for combined MPTs indicating abnormal glucose e.g. aggravated DM and impaired glucose tolerance, but were as expected for combined MPTs relating to inadequately controlled diabetes. Data for quetiapine and ziprasidone were inconclusive. Risperidone and haloperidol were indistinguishable from each other and had lower EBGM scores overall than other agents.

Conclusions: Although spontaneous report data should be interpreted with caution, these results suggest antipsychotics have very different glucose-related adverse-effect profiles and do not support a "class effect" hypothesis.

Funding Source(s): Janssen Pharmaceutica Products, LP

References:


NR910 Thursday, May 6, 12:00 p.m.-2:00 p.m.

A Self-Report Rating Scale to Screen for Psychiatric Disorders

Joyce Sprafkin, Ph.D., Psychiatry Department, State University of New York, Putnam Hall, South Campus, Stony Brook, NY 11794; Kenneth D. Gadow, Ph.D., Jayne Schneider, Ph.D.

Educational Objectives:

At the conclusion of this session, participants should be able to describe evidence of the reliability and validity of the ASRI-4 and to describe how the ASRI-4 can be useful as a screen for psychiatric disorders.

Summary:

Objective: There is a need for efficient rating scales to help psychiatrists screen for a wide range of DSM-IV disorders in adults. This study examines the reliability and convergent/discriminant validity of the Adult Self-Report Inventory-4 (ASRI-4).

Method: A community sample of 378 males and 435 females (18–75 years) anonymously completed the ASRI-4. Participants also completed a set of other validated measures that assess similar constructs as those in the ASRI-4 (e.g., Brief Symptom Inventory; Social Phobia Inventory; Eating Attitudes Test; PTSD Checklist; Mood Disorder Questionnaire; Screening Test for Somatization Disorder). A subsample (N=219) completed the ASRI-4 a second time two weeks later.

Results: Test-retest correlations ranged between .61 and .94 (M=.74). Correlations between ASRI-4 categories and the validity-evidence scales showed a fairly predictable pattern of convergence with scales containing similar symptoms and divergence with scales of dissimilar symptoms.

Conclusions: Based on these preliminary findings, the ASRI-4 is a reliable and valid measure to screen for many psychiatric disorders in adults.

Funding Source(s): Subject payments funded by Checkmate Plus.

References:


NR911 Thursday, May 6, 12:00 p.m.-2:00 p.m.

Validity of Norm-Referenced Self-Report Scale of DSM-IV Symptoms in Adults

Jayne Schneider, Ph.D., Psychiatry Department, State University of New York, Putnam Hall, Stony Brook, NY 11794-8790; Joyce Sprafkin, Ph.D., Kenneth D. Gadow, Ph.D.

Educational Objectives:

At the conclusion of this session, participants should be able to describe how a norm-referenced, self-report rating scale can facilitate diagnostic evaluations of DSM-IV disorders.

Summary:

Objective: Although there are several self-report rating scales of DSM-IV disorders in adults, none are norm-referenced. Norm-based scoring (i.e., T scores) adds an important feature to traditional diagnostic criteria.

Method: Two groups of adult participants, a normative sample (N=711) and a clinic sample (N=492) completed the Adult Self-Report Inventory-4 (ASRI-4), a rating scale of DSM-IV psychiatric symptoms.

Results: Cronbach’s alphas for the 15 ASRI-4 symptom categories (>3 items) were satisfactory for both normative (mean=.81) and clinic (mean=.84) samples. Low to moderate intercorrelations were generally found among ASRI-4 symptom categories in both samples, which supports the notion that they measure different clusters of symptoms. For most symptom categories, the clinic sample received significantly higher severity scores than the normative sample for Axis I (e.g., depression, anxiety, bipolar, schizophrenia, ADHD) and Axis II (e.g., antisocial, borderline) disorders. Gender differences were comparable in both samples. The clinic sample evidenced a pattern of moderate (65 ≤ T ≤ 69) or high (T ≥ 70) symptom severity consistent with their clinical status and diagnoses in both males and females.
Conclusions: Results indicate that the ASRI-4 is a useful self-report measure for assessing the severity of psychiatric symptoms (relative to a normative sample) in clinic-referred adults.

Normative sample participant honoraria funded by Checkmate Plus.

References:

NR912  Thursday, May 6, 12:00 p.m.-2:00 p.m.
Topiramate Efficacy in Migraine Prevention: Data From Two 26-Week Trials
Supported by Johnson & Johnson
Alvin E. Lake III, Ph.D., Michigan Head Pain & Neurological Institute, 3120 Professional Drive, Ann Arbor, MI 48104-5131; Grace Forde, M.D., Stefan Schwabe, M.D., Daniel Wang, Ph.D., Jennifer Schmitt, M.S.

Educational Objectives:
At the conclusion of this session, the participant should be able to evaluate the evidence for clinical efficacy of topiramate as a migraine preventive and identify potential adverse effects.

Summary:
Introduction/Hypothesis: Migraines are highly prevalent in the general population and may also occur in patients presenting with psychiatric illnesses. Traditionally, responders to migraine preventives are defined as showing >50% reductions in attack frequency. Topiramate efficacy in preventing migraines was assessed across two placebo-controlled trials.

Methods: Efficacy measures for the pooled intent-to-treat population (N=937; 88% female; mean age=40y) included mean monthly migraine frequency change and categorical response rates.

Results: Significantly reduced mean monthly migraine frequencies were observed throughout the entire double-blind phase for 100mg/d topiramate (~2.1 migraines/month, least-squares mean) and 200 mg/d topiramate (~2.3), vs placebo (~1.2), P<0.001. Median percent changes in migraine frequency were 50.7% and ~48.9% for 100mg/d and 200 mg/d topiramate respectively (~20.7% for placebo). Significant percentages of patients receiving 50mg/d (37.3%), 100mg/d (51.6%) or 200mg/d topiramate (49.6%) exhibited ≥50% monthly migraine frequency reduction vs placebo (23.1%, P<0.001). Significant percentages of patients receiving 50mg/d (18.9%), 100mg/d (26.6%) or 200mg/d topiramate (25.9%) exhibited ≥75% reduction vs placebo (10.5%, P<0.01). The most common AEs in controlled topiramate migraine prevention studies are paresthesia, fatigue, anorexia, nausea, taste alteration, diarrhea.

Conclusions/Discussion: Topiramate significantly reduces migraine frequency. Significant numbers of patients receiving topiramate met and exceeded traditional responder rates (≥50% and ≥75% reductions in attack frequency). 100mg/d topiramate should be targeted for efficacy/tolerability in most patients.

Research funded by Johnson & Johnson Pharmaceutical Research & Development.

References:

NR913 Thursday, May 6, 12:00 p.m.-2:00 p.m.
GADISS II Study in Belgian Primary Care Confirms the Existence of Sociocultural Risk Factors Besides Socioeconomic Factors in Prevalence of GAD and Major Depression
Supported by Wyeth Pharmaceuticals
Benjamin Fischer, M.D., Department of Infectious Diseases, St. Pierre Hospital, Rue de Namur 77-9, Brussels 1000, Belgium; Marc Ansseau, M.D., Sophie Leyman, M.D., Michel Dierick, M.D., Annick Mignon, Adelin Albert, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize the risk factors for the presence of GAD and depression in primary care and be aware that region is an independent risk factor in addition to socio-economic factors.

Summary:
Objective: The first Generalized Anxiety and Depression Impact Survey (GADIS I) (n=13135) demonstrated major differences in the prevalence of MD and GAD in primary care between Belgian regions (Flanders, Wallonia and Brussels Capital). GADIS II aimed at assessing the relative impact of cultural and socio-economic factors on such differences.

Methods: Using an internationally validated structured psychiatric interview (MINI), 377 general practitioners assessed MD and GAD in 40 consecutive patients (total 12819 patients). Demographic, cultural, socio-economic, and therapeutic data were collected.

Results: MD and/or GAD was more prevalent in Wallonia (22.7%) and in Brussels Capital (24.2%) than in Flanders (12.9%). By multivariate logistic regression analysis, age, gender, living status (single or not), and professional status (unemployed or not) but also region were significantly associated with GAD and MD. Significant interactions were also found between region and socio-economic factors. The risk of MD/GAD was lowest (9.4%) for married, employed men living in Flanders and highest (44.5%) for single, unemployed women living in Brussels Capital. About 50% of the patients still diagnosed with MD/GAD were already under treatment.

Conclusions: GADIS II confirmed the existence of subgroups of subjects at risk of MD/GAD in the Belgian Primary Care setting and demonstrated that socio-economic factors only partly explain existing regional differences.

Funding Source(s): GADIS II was funded by Wyeth pharmaceuticals Belgium

References:
NR914  Thursday, May 6, 12:00 p.m.-2:00 p.m.
The Use of PRIME-MD for Diagnosing Depression in a Medical Setting in Brazil

Sergio Henriques, Jr., M.D., Psychiatry Department, Psychiatry Institute, Rua Ovidio Pires de Campos 5YN(sin), Sao Paulo, SP 05403-010, Brazil; Renerio Fraguas, Jr., M.D., Pavlo R. Menezes, M.D., Mara de Lucia, Ph.D., Wagner F. Gattaz, M.D., Robert L. Spitzer, M.D.

Educational Objectives:

At the conclusion of this session, participants should be able to recognize the utility and make better use of an instrument for diagnosing depression in medical settings.

Summary:

Objective: to evaluate the utility of PRIME-MD in diagnosing depression for clinical and research purposes in a medical setting in Brazil.

Method: 578 consecutively admitted patients from a teaching outpatient care unit of a teaching general hospital were evaluated by general practitioners using the PRIME-MD, and 347 of them were also evaluated by psychiatrists using the SCID. A checklist was used to assess clinical parameters, absenteeism and utilization of health care services. Data were analyzed using a discrepancy table, the kappa statistics and correlation tests.

Results: Major depression was diagnosed in 225 (39.6%) patients. It was more prevalent in women (p = 0.003), in patients younger than 57 years (p = 0.01), and was associated with more days of absenteeism (p = 0.04). Discrepancies greater than 4 depressive symptoms between PRIME-MD and SCID occurred in 18 (6.27%) patients. The kappa statistics for major depression was 0.92 among the most severe cases and the mildest ones (those with 0, or 8 and 9 symptoms), 0.68 for those with 0, 1, 2, 8 and nine symptoms, 0.47 for the sample as a whole, 0.52 for men, and 0.37 for women.

Conclusions: using the PRIME-MD, general practitioners showed low discrepancy for more than 4 symptoms. Agreement in the diagnosis among severe and mild cases was very good. The high prevalence in the medical setting of subjects on the boundaries of the diagnostic criteria for major depression, i.e., three to seven symptoms, increases the risk of misdiagnosis. For clinical purposes we suggest that the primary care physician should consider the possibility of a depressive disorder in any patient with three or more depressive symptoms. For research purposes the severity of depression, and not only its diagnosis alone, should be taken into account.

Funding Source(s): Fundacao de Amparo a Pesquisa do Estado de Sao Paulo-FAPESP

References:

NR915  Thursday, May 6, 12:00 p.m.-2:00 p.m.

Efficacy and Safety of Sertraline Treatment of Neurasthenia

Supported by Pfizer Inc.

Jianping Chen, M.D., Mental Health Department, CBW Health Center, 268 Canal Street, 3rd Floor, New York, NY 10013

Hong Chen, Ph.D., Susan Seto-Yee, M.P.A., Henry Chung, M.D.

Educational Objectives:

At the conclusion of this session, the participant should understand the diagnostic importance of neurasthenia among Asian Americans, and assess the utility of using a selective serotonin reuptake inhibitor (SSRI) for the treatment of neurasthenia.

Summary:

Introduction: Neurasthenia is a cultural syndrome that is diagnosed commonly in East Asian countries, and has been seen as a cultural variant of depression. However, the syndrome is distinct in that it is not necessary to have mood symptoms, and instead has fatigue as its core symptom. There are no published studies that have assessed the safety and effectiveness of using an SSRI for its treatment.

Methods: Subjects who met diagnostic criteria for neurasthenia with or without depression and/or dysthymia were enrolled in a 13-week, open-label study with flexible dosing of sertraline 50–200 mg. The primary efficacy measures were the CGI-I, and the Multidimensional Assessment of Fatigue Questionnaire (MAFQ). Secondary measures included the Patient Health Questionnaire, Somatic Symptoms Inventory, Hamilton Anxiety Scale, and the Quality of Life, Enjoyment, and Satisfaction Questionnaire.

Results: 19 subjects were available for baseline to endpoint intent-to-treat analysis. The mean CGI-I mean change score was -1.9 ± 1.2, (p < 0.0002), 47% of subjects were CGI-I responders (CGI-I ≤ 2). The mean MAFQ change score -20.2 ± 18.1 (p < 0.0001). In the completer subgroup (n = 10), the mean change in CGI-I was -1.9 ± 1.2, (p < 0.0007) and 80% were CGI-responders. The mean MAFQ change score was -29.4 ± 18.1, (p < 0.0008) 2 subjects discontinued the study due to adverse events and no serious adverse events occurred.

Conclusion: Sertraline was generally well tolerated and effective for the treatment of neurasthenia in this pilot study. A larger, controlled study should be performed to confirm these findings.

Funding Source(s): Pfizer Inc, Investigator Initiated Grant

References:

NR916  Thursday, May 6, 12:00 p.m.-2:00 p.m.

Screening for Depression and Anxiety in Chilean Patients With Rheumatoid Arthritis

Jorge B. Barros, M.D., Department of Psychiatry, University Catolica, Camino El Alba 12351 Las Condes, Santiago, Chile; Loreto Massardo, Paula Pizarro, Ximena Velasquez, Claudia Pizarro, Mariana Sinning, Sergio Jacobelli

Summary:

Objective: To determine the presence of major depression (MD) and anxiety in sample of patients with rheumatoid arthritis (RA).

Methods: MD and Anxiety 75 patients with RA were established using the structured interview from the Center for Epidemiological Studies-Depression and Anxiety (CIDI). The Zung self rating scale for depression was also used. Severity of symptoms was assessed with the Hamilton Scale.

Results: Most of the 75 RA were Women (n = 70), middle aged (median 55), married (73%), housewives (51%), and had active disease at the interview (82%). Depression (CIDI) was found in...
35 (47%) of RA patients. Symptoms according to the Hamilton scale were severe in 37%, moderate in 39% and mild in 24% of patients. Anxiety was found in only 6 (15%) of the 40 patients without depression. Patients with depression had longer disease duration (p < 0.04) or ACR functional class (p < 0.05). The reliability of the Zung scale showed a good internal consistence (Cronbach's alpha coefficient of 0.8696).

**Conclusion:** In a search for psychiatric disorders in patients with RA, only MD associated with the disease in this series. The frequency of MD was 47%, higher than the 15% for British and the 35% of Spanish series from RA patients, and of the general population of Santiago. The Zung scale may be a useful test to screen for MD in an outpatient basis.

**Funding Source(s):** Department of Psychiatry, Loyeth

**Summary:**

**Objective:** To compare the efficacy of 2 once-daily formulations of methylphenidate (MPH) over 8 hours in children aged 6 to 12 with attention-deficit/hyperactivity disorder (ADHD).

**Method:** Data were pooled from 2 similarly designed, single-blind, crossover studies that randomized children with ADHD to alternately receive 1 day of treatment with 20-mg MPH extended-release capsules (MPH-ER; Ritalin™, Novartis Pharmaceuticals, East Hanover, NJ), 18-mg or 36-mg MPH modified-release tablets (MPH-MR; Concerta®, ALZA Corporation, Mountain View, Calif), and placebo at weekly intervals. Efficacy was evaluated in a laboratory classroom using SKAMP scores and written math tests (questions attempted, questions answered correctly), expressed as area under the curve (AUC) for change from predose scores. Efficacy was evaluated in 55 children who had previously been stabilized on 20 mg or less immediate-release MPH.

**Results:** Both AUC<sub>0.4</sub> and AUC<sub>0.8</sub> for SKAMP-Department, and Math Test-Correct were significantly greater with MPH-ER-20 than with each dose of MPH-MR (P≤0.034). In Math Test-Attempts, MPH-ER-20 was significantly superior to each dose of MPH-MR in AUC<sub>0.4</sub> (P≤0.021) and to MPH-MR-18 in AUC<sub>0.8</sub> (P=0.043).

**Conclusion:** For 8 hours after a single dose, MPH-ER-20 offers significant behavioral and cognitive advantages over MPH-MR-18 and MPH-MR-36.

**References:**


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